The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 118, No. 12 — CHICAGO, ILLINOIS — MARCH 21, 1942

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TREATMENT OF ARTHRITIC JOINTS

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BOSTON

ARTHRITIC JOINTS

One still hears too frequently the neglected cripple, on seeking hospital care, declare that her physician despairingly admitted to her or to members of her family that she had arthritis and that there was no treatment which would help her. It is to that physician in whatever community he may reside that this paper is written.

Some idea of the relative importance of rheumatism may be gained from the estimated prevalence of specified chronic disease in the United States in 1937,[1] shown in the accompanying table.

In Massachusetts alone, out of a population of about 4,250,000 in 1930, there were 140,000 persons [2] found afflicted with this "king of human misery." Today it represents our greatest single cause of chronic disease. Yet four fifths of the poor and one half of the well-to-do who were suffering from chronic disease were not under the care of any physician.

In most forms of arthritis the joint symptoms are only manifestations of a systemic disease. Therefore the care of the patient should not be relegated to one physician but to a group consisting of an able, interested internist who should work with the aid of the orthopedic surgeon, the physical therapist, the occupational therapist and, in many instances, the psychiatrist.

Deformities may be prevented by simple orthopedic management, which, to a certain extent, can be carried out by any physician who realizes the danger from neglect and who knows how to apply preventive measures. An ounce of early well directed care to prevent deformities and relieve pain until the disease process is quiescent is worth tons of reconstructive work later. It avails one little or nothing to arrest or cure the disease process and have deformed joints that doom the patient to the life of a cripple. Such a patient can never become self sufficient without a long program of joint rehabilitation and correction.

The care of the joints in arthritis regardless of the cause has been a neglected subject. A great deal has been written concerning the physiologic and pathologic changes in articular structures, but only a few papers have appeared in recent years that give the physician any help in dealing with these complex structures. In the first place, accuracy in diagnosis is of paramount importance for both treatment and prognosis. The present acceptable working classification is based on the cause:

Origin known:

1. Traumatic; e. g., due to internal derangements of joints, fractures into joints, and so on.
2. Infectious; e. g., due to the tubercle bacillus, gonococcus, streptococcus, staphylococcus or other organism.
3. Neuropathic; e. g., due to tabes, syringomyelia, leprosy, or other disease.
4. Arthritis associated with metabolic or constitutional diseases; e. g., hemophilia, gout.
5. Anaphylactic or allergic; e. g., associated with serum sickness.
6. "Fibrositis," "fascitis," tenosynovitis, and so on, of known origin.

Origin not certainly known:

1. Rheumatoid, proliferative or atrophic arthritis.
2. Hypertrophic, degenerative or osteoarthritis.
3. Rheumatic fever.
4. "Fibrositis," "fascitis," tenosynovitis, and so on, of unknown origin.

Most deformities occur in the rheumatoid type for which there has been offered no satisfactory or acceptable etiology; consequently there is no specific means of therapeutic attack. Nevertheless, certain general principles have proved valuable in preventing deformities. Even in those groups in which the cause is known or suspected, the joints must be adequately cared for while the offending agent is being attacked by other means.

As a general rule, flexion deformities are the ones to be guarded against. The aims in the care of joints should be prevention of deformities and preservation of as nearly normal joint motion as possible.

Rest, unquestionably, is the sheet anchor in the orthopedic management of arthritic joints. Comfortable support to the affected part should be provided in a neutral position or in a position for optimum use should the joint eventually become limited in motion or ankylosed. Active or guided motion (without injury) must be employed daily in an effort to retain as much motion as possible: first, by preventing the formation of adhesions within the joint; second, by preventing contractures of periarticular structures, and, third, by providing a stimulus to the articular cartilages.

If a patient with painful joints due to arthritis is placed in bed and left there without proper care, the extremities eventually assume well recognized deformities. Extensive atrophy takes place in the muscles, bones and joint cartilages because little motion can be performed in painful limbs which are held rigid by con-

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1. Osgood, R. B.: The Medical and Social Approach to the Problem of Chronic Rheumatism, Am. J. M. Sc. **200**: 429 (Oct.) 1940.
2. Bigelow, G. H., and Lombard, H. L.: Chronic Rheumatism in Massachusetts, New England J. Med. **203**: 1232 (Dec. 18) 1930.

stant muscle spasm. Even in normal joints the cartilage becomes atrophic if the parts are immobilized for long periods of time.[3]

In this paper individual joints have been considered separately except in certain instances in which several joints have been grouped together for obvious reasons. One objection to this form of presentation is that repetition of certain forms of treatment is bound to appear. Nevertheless, we feel that the advantages of this method outweigh its disadvantages.

Fig. 1.—Shoulders supported with pillows in abduction and external rotation.

Chronic Diseases in the United States in 1937

Diseases	No. of Cases
Rheumatism	6,850,000
Heart disease	3,750,000
Arteriosclerosis and high blood pressure	3,750,000
Nephritis and other kidney diseases	1,550,000
Nervous and mental diseases	1,450,000
Cancer and other tumors	930,000
Tuberculosis, all forms	680,000
Diabetes mellitus	660,000

SHOULDER

In attempting to avoid shoulder deformities, one should restrict the use of excessive pillows beneath the head, neck and back in reclining or semireclining positions. The bed should be as flat and firm as tolerated, and only a small pillow, if any, should be allowed beneath the head. The patient should be taught to lie with his hands clasped beneath his head for short periods several times daily, since this position permits shoulder abduction and external rotation.

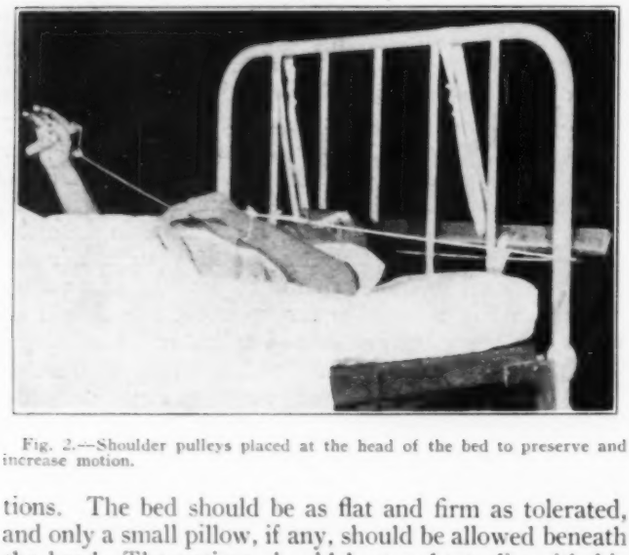

Fig. 2.—Shoulder pulleys placed at the head of the bed to preserve and increase motion.

In arthritis of the shoulder there is frequently a tendency to forward drooping with adduction and internal rotation of the arm. This may be prevented by supporting the arms with pillows, sandbags or plaster splints in a moderate amount of abduction and external rotation (fig. 1). Codman [4] has taught that adhesions form less readily in this position. If the shoulder is the only joint involved and the patient is otherwise ambulatory, an airplane splint may be used.

During the stage of acute activity, hot fomentations applied to the shoulders greatly relieve pain and muscle spasm and permit freer motion. It is important to remember that after the fomentations are applied the shoulder should be passively guided or actively moved at least twice daily through as full a range of motion as is possible, to prevent adhesions. Shoulder pulleys (fig. 2) or screw eyes fastened to ends of a board, attached to the head of the bed, constitute a useful and simple device to assist active motion in the acute stages. Ordinary awning pulleys or screw eyes and awning rope may be obtained from the local 5 and 10 cent stores.

Fig. 3.—A molded plaster splint for resting the upper extremity.

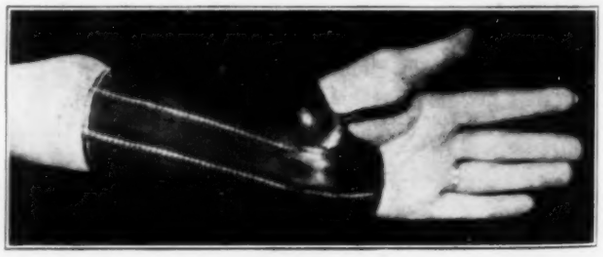

Fig. 4.—Removable leather cock-up splint for the wrist.

In the quiescent period, deformity and limitation of motion may be corrected by using the same device, by gradual stretching after heat and massage or by the aid of occupational therapy, such as the use of looms and other exercises designed to promote shoulder motion.[5] If such conservative methods fail, manipulation under anesthesia, if gently performed, is a safe and effective method to secure an increased range of motion. The manipulated joint must be moved twice daily through its new range to prevent adhesions reforming.

3. Green, W. T., and Ober, F. R.: Chronic Arthritis in Children, Proc. Am. A. for the Study and Control of Rheumatic Disease, first annual meeting, third conference, Cleveland, 1934.

4. Codman, E. H.: Boston M. & S. J. **165**: 115 (July 27) 1911.

5. Joplin, R. J.: Application of Principles of Posture in Occupational Therapy, Occup. Therapy **20**: 1 (Feb.) 1941.

Actual ankylosis of the shoulder joint is rare but does occur. Restoration of motion requires surgical intervention.

ELBOW

One reason why the elbow joint is so frequently attacked in arthritis is probably that it is misused. Although it is normally a non-weight bearing joint, when the patient begins to support himself by holding on to chairs, tables or by using a cane the elbow becomes a partial weight bearing structure. Such misuse constitutes trauma. Especial vigilance is needed to prevent deformity or limitation of motion.

During the acute stage the patient carefully holds his elbow in the protective position of flexion. Should he be confined to bed, the elbow is usually held at an angle

Fig. 5.—Permanent cock-up splint for wrist, made of castex.

Fig. 6.—Arthritic deformity of hand showing characteristic ulnar deviation and subluxation of the fingers.

of 90 degrees or less with the hand in pronation resting on the chest. This is the customary position these patients assume during sleep in order to assure themselves a little comfort.

Treatment during this stage (fig. 3) consists in resting the entire arm and hand in a molded plaster splint with the elbow in as much extension as can be tolerated. The arm should rest in this support most of the time but may be removed several times daily to allow guided or active motion. If ankylosis appears to be taking place in spite of adequate therapy, the joint should be allowed to fuse in a useful position, which is slightly less than a right angle with the forearm in supination or midway between supination and pronation.[6]

After the disease has become quiescent, some of the limitation of motion may be overcome by the use of hot fomentations followed by gentle manual stretching or by allowing the patient to carry weights. Traction often proves effective when other measures have failed. Manipulation under anesthesia is seldom satisfactory because increased stiffness frequently follows. If com-

Fig. 7.—Cock-up plaster splint to correct ulnar deviation of the hand and fingers.

plete ankylosis has occurred in a bad position and motion is greatly desired an arthroplasty may be resorted to, provided the disease has become quiescent.[7]

WRIST

When the wrist is involved, deformity results from the overpowering pull of the flexor muscles, aided by gravity, in keeping the joint palmar flexed. This position tends to diminish the hand's normal grasping power. Furthermore, the position of comfort assumed by arthritic patients confined to bed, namely with the hands resting across the chest, leads not only to flexion of the wrist but to ulnar deviation of the hand as well. This deformity may be easily prevented by the use of cock-up splints made of various kinds of splinting material, such as plaster of paris, leather (fig. 4) or castex (fig. 5). The advantages of the castex wrist support are many, for it can be applied next to the skin without padding and left in place for weeks at a time. Since it is waterproof, it does not restrict one's ordinary functions. For example, a housewife can wash dishes with the splint on. Such a support worn constantly has proved more effective for this joint than one that is removable.

Fig. 8.—Paraffin wax being applied to hand.

The "optimum angle" of the splint should be about 30 degrees in dorsiflexion. These splints should extend from the upper forearm down to the palmar crease to permit active use of the hand if the fingers are not involved. If the fingers are swollen and painful, the splint may include the fingers and thumb as well. One should be cautioned against

6. Campbell, W. C.: Operative Orthopedics, St. Louis, C. V. Mosby Company, 1939.

7. Roberts, S. M., and Joplin, R. J.: Arthroplasty of the Elbow, New England J. Med. **216**: 646 (April 15) 1937.

making a so-called "chimpanzee type," or flat, hand. To avoid this the thumb must be placed in a position of apposition.

During the acute stage the splint may be worn constantly or, preferably, it may be removed at least once daily to allow motion or to permit other local therapeutic measures. In milder cases, however, the splint may be worn only at night. Such splinting greatly relieves pain, congestion and swelling. The use of hot fomentations during the acute stage aids in relieving pain and muscle spasm, which in turn lead to increased motion.

If deformity has already occurred, gradual correction by a series of cock-up splints, starting in the line of deformity and gradually bringing the wrist into dorsiflexion, as tolerated by the patient, often results in gaining increased motion. Should ankylosis appear

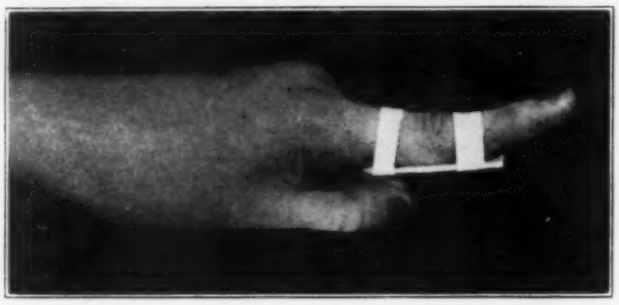

Fig. 9.—Holding of reduction by wooden splint fastened with adhesive tape.

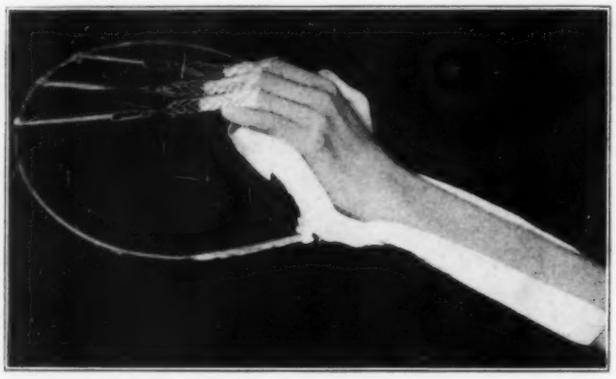

Fig. 10.—Banjo splint with wire mesh finger stalls used to reduce subluxating interphalangeal joints.

inevitable, the wrist should be allowed to fuse in a useful position. Manipulation under anesthesia may be necessary to secure sufficient correction before the bones become firmly united. If ankylosis has taken place in a bad position, operative correction with fusion in 30 degrees dorsiflexion is most desirable.

HANDS

It is a most pitiful sight to watch an arthritic patient try to do simple chores when his fingers are in the deformed position of fixed ulnar deviation (fig. 6) and subluxation. These deformities greatly diminish the hand's functional usefulness and discourage dexterous efforts. The normal axis of rotation in flexion of each finger has been so changed that instead of their converging and pointing normally to the tubercle of the scaphoid they point more toward the pisiform bone. Furthermore the accompanying atrophy of the interossei and the lumbricales muscles results in dorsiflexion (or hyperextension) of the metacarpophalangeal joints, flexion of the proximal interphalangeal joints and hyperextension of the terminal interphalangeal joints.

A splint (fig. 7) well molded into the palmar arch and extending beyond the partially flexed fingers may prevent these deformities. Ulnar deviation may be

Fig. 11.—"Clam shell" plaster cuff used to prevent and correct subluxation of metacarpophalangeal joints.

avoided or corrected with the same splint by incorporating a flange on the ulnar edge or by making a paster mitten into which the tips of the fingers fit snugly.

In both the acute and chronic stages of the disease, dipping the hand (fig. 8) in paraffin wax melted in a double boiler or pail is a most effective means of applying heat for the relief of pain and muscle spasm.

Paraffin wax is admirably adapted for this purpose since it has a hysteresis of about 15 degrees. Although its melting point is uncomfortably warm to one's touch, a container of melted wax may be allowed to cool until a thin film forms over its surface. At this point one can thrust one's hand into the liquid and instantly remove it without experiencing any discomfort. The resulting coating solidifies on exposure to the air. The hand may be dipped in and out of the pail four or five times to secure a thick glove. The heat slowly dissipates from the waxed glove in about one-half hour. It can then be peeled from the hand and replaced in the pot to be reused.

Fig. 12.—Corset recommended for back support.

After the use of heat, the preservation of motion may be maintained by daily voluntary exercises: i. e., by flexing the fingers well into the palms of the hands and also bringing them into complete extension. A good finger and hand exercise results from simply squeezing a rubber ball or a rubber sponge several times daily. Also, when recovery is sufficiently advanced, the use of occupational therapy, such as needle work, cord weaving, putty molding or wood carving, will greatly increase motion and promote dexterity.[8]

8. Marble, Henry: Rehabilitation Hand Clinic at Massachusetts General Hospital, personal communication to the authors in September 1940.

When subluxation of the interphalangeal joints has taken place, this may be corrected by simple manual traction and the reduction gained held by small wooden splints cut from throat sticks and fastened in place on the palmar surfaces of the fingers with adhesive tape (fig. 9). Banjo splints (fig. 10) with adhesive finger traction, or the use of wire mesh finger stalls, are also useful.

One of the simplest splints, yet one of the most effective in preventing the interphalangeal as well as metacarpophalangeal subluxations, is the so-called "clam-shell" cuff (fig. 11) devised by Dr. Loring T. Swaim. It consists of a piece of felt and a plaster slab molded and allowed to harden about the subluxed joints in their corrected positions. After it has been allowed to dry, it is held on the hand with a webbing strap or an elastic band. It can be slipped off and on with ease.

Another common deformity is the aforementioned "flat hand" which is accompanied by the loss of the

Fig. 13.—Low spring steel back support with elastic shoulder straps.

palmar arch. This is caused by too much weight bearing on the outstretched hand, as in getting up from the bed or chair or by the faulty use of crutches. Prevention lies in teaching the patient the correct use of crutches and stressing the use of the hand in a grasping position of dorsal flexion rather than in extension. A cock-up splint, well molded into the palmar arch, or a snug fitting wrist strap that encircles the carpal bones is useful in treating this deformity.

If a hand must be stiff, the most useful position is one with dorsiflexion of the wrist, flexion at the metacarpophalangeal joints, partial flexion of the fingers and apposition of the thumb.[9] If one remembers these criteria, preservation of some function of this important extremity will be preserved.

SPINE, NECK AND JAW

By far the largest number of painful backs fall into the so-called hypertrophic or osteoarthritic group. These patients are usually beyond middle age. The roentgenogram reveals lipping or spurs at the ligamentous attachments. Treatment is relatively simple. These patients respond readily to heat, rest, support and correction of malposture, if this exists. Bed rest is

Fig. 14.—Apparatus for traction of cervical spine.

seldom indicated. Adhesive strapping usually gives immediate temporary relief. For women, back laced, nonelastic, supporting corsets (fig. 12) are usually sufficient. Occasionally an obese patient or one with more severe symptoms may require a flexible steel back brace with a firm abdominal pad in addition (fig. 13). Elastic shoulder straps may be added if the thoracic spine is involved. For men a back brace of exactly the same type is used except that peroneal straps may be substituted for the garters.

Whenever the vertebral joints are attacked in the rheumatoid or atrophic type of arthritis the resulting deformity is flexion, especially in the dorsal spine, with a tendency to reverse the normal lumbar curve. In the Marie-Strümpell type, which attacks the younger age group, the sacroiliac joints are affected first and often fuse solidly before the spinal column becomes involved.[10] As the disease progresses, the rib articulations are attacked with the resultant limitation of chest motion and diminished vital capacity. The cervical spine has a tendency to flex forward until gradually the patient loses the ability to carry his head erect. Likewise the patient loses his ability to turn to either side without moving the entire body as a whole. A scoliosis rarely appears.

Fig. 15.—Light weight ambulatory hip spica.

During the acute phases, hot fomentations and bed rest are desirable measures because they afford relief from muscle spasm and pain. Later, considerable relief

9. Steindler, Arthur: Orthopedic Reconstruction Work on Hand and Forearm, Surg., Gynec. & Obst. **45**: 476 (Oct.) 1927.

10. Swaim, L. T.: The Orthopedic Treatment of Strümpell-Marie Arthritis, J. Bone & Joint Surg. **21**: 983 (Oct.) 1939.

is afforded these patients by the continuous use of a rigid body jacket to immobilize the spine and to prevent deformity. In cases in which deformity already exists, such a jacket may aid in straightening the spine.[11] Swaim points out that the use of a rigid support of this

Fig. 16.—Plaster splint for resting lower extremity.

type not only corrects and prevents deformity but shortens the course of this disease.

It is important that these patients with spinal arthritis rest in bed on firm, even surfaces, because this in itself will tend to prevent flexion deformities. A three ply board, ¼ inch thick and 3 by 5 feet in size, for a single bed, placed between a thin hair mattress and the springs, will be found to be more comfortable than a thick soft bed.

If the patient is bedridden a simple plaster mold for the back may be sufficient, but the use of a rigid body jacket is better. The jacket should be laced in front to allow its removal once or twice daily for heat treatments to the spine and for the bath. It permits the patient to roll over in bed or to move about more freely.

Fig. 17.—Caliper splint used to maintain and gain correction in flexion deformities of the knee.

In cervical arthritis a rotation or lateral tilting of the head occurs occasionally. This deformity is not only unsightly but prevents normal vision. Such a torticollis may be prevented by the use of a Thomas collar or a simpler device known as a Wallace collar, or by the use of a medium sized turkish bath towel folded twice lengthwise, wrapped around the neck two or three times, and held in place by safety pins.

If the patient is confined to bed, the head may be held in place by sandbags. If the pain is severe or if deformity has already occurred, traction (fig. 14) may be resorted to; and the correction thus gained may be retained by the use of sandbags. Heat in the form of hot fomentations is efficacious in relieving the muscle spasm and pain.

11. Joplin, R. J.: Technic of Making a Light Waterproof Jacket for the Treatment of Arthritis of the Spine, Am. College Surg., Library of Motion Picture Films, Chicago, 1939.

Although arthritis of the temporomandibular joint occurs frequently, ankylosis is rare; but limitation of motion is frequent. The chewing of gum after the acute symptoms have abated tends to prevent limitation of motion.[12] Wooden or cork wedges inserted between the teeth may be found helpful in increasing the range of motion. Because arthroplasty of this joint is attended with a high degree of success, it is resorted to occasionally in the most severe cases.[6] It is a difficult procedure which should be performed only by one accustomed to operating in this field.

HIP

Pain referred to the anterior thigh and mesial aspect of the knee may be the first symptom of arthritis of the hip. Examination may reveal a slight permanent flexion deformity and, after exercise, some muscle spasm.

Permanent flexion deformity with muscular atrophy is inevitable unless it is prevented by proper measures. Either prevention or correction of permanent hip flexion may be obtained by having the patient lie prone in bed at least once each day, starting with one or two pillows beneath the abdomen. As the pillows are gradually removed, the hip will assume a neutral position from the stretching of the anterior structures. Slight flexion deformities can be corrected by hot fomentations accompanied by traction in the line of deformity.

Fig. 18.—Plaster cylinders for knee support.

A simple device to preserve muscle tone may be arranged by supporting the leg in a padded canvas cuff suspended by an elastic cable from an overhead bed frame. The patient can do so-called bicycle exercises almost as effectively as though he were placed in a Hubbard tank.[13]

A plaster cast in the form of a unilateral or bilateral spica is effective in securing relief from an acutely painful joint. It may be used also in correcting any deformity that may have taken place, provided it is changed or altered frequently until a good position is secured. In atrophic or rheumatoid arthritis, long immobilization in one position may produce diminished motion, but in osteoarthritis or hypertrophic arthritis there is less danger of such stiffness resulting. When a good position is obtained a permanent, ambulatory type of light weight spica (fig. 15) may be worn. This may be removed at times to permit active or guided motions and other physical therapeutic measures.

12. Bayles, T. B., and Russell, L. A.: The Temporomandibular Joint in Rheumatoid Arthritis, J. A. M. A. **16**: 2842 (June 28) 1941.

13. Elliston, W. A.; Silber, Marie F., and Grover, Dorothy: Physiotherapy in Rheumatoid Arthritis, New England J. Med. **224**: 150 (Jan. 23) 1941.

If painful hip motion is still present after conservative therapeutic measures have been exhausted, or, if ankylosis has occurred in a poor position, an arthroplasty with a vitallium cup[14] may give a painless, movable joint. When ankylosis is inevitable and the general condition of the patient does not warrant an operation, the hip should be allowed to fuse in slight flexion, without rotation, and in about 10 degrees abduction.[6]

KNEES

The knee is the largest joint in the body. Because it is a weight bearing structure it is frequently attacked. The first signs of impending deformity are pain, swelling and permanent flexion.

Atrophy of the muscles and ligaments about the joint appears rapidly. Subluxation of the tibia on the femur may occur as the fluid subsides. The joint space usually becomes narrowed and the patella is often fixed against the femoral condyles, where fusion occasionally takes place. Contracture of the hamstring muscles, joint capsule and periarticular structures results. Ankylosis in chronic arthritis, especially of the osteo or hypertrophic type is rare but it frequently follows the acute suppurative joint disease such as that due to gonorrhea.

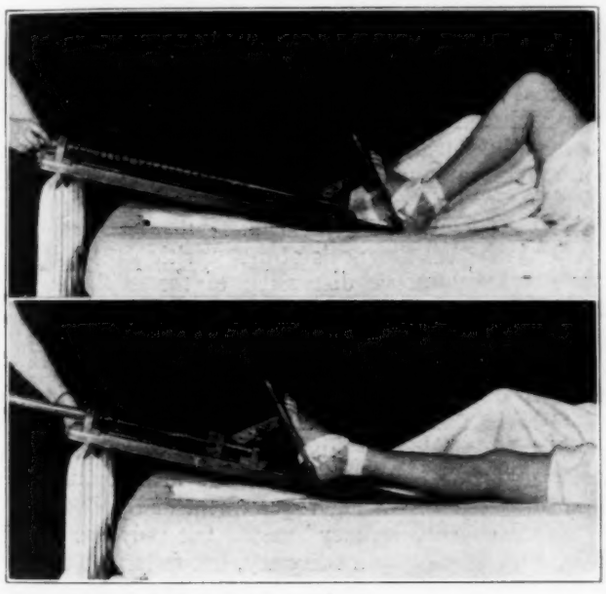

Fig. 19.—So-called "knee-push machine," consisting simply of a board on which a foot rest slides in a dovetail groove. A coil spring wound around a wooden pole which slides through a stationary end block provides slight resistance.

In the acute stage of rheumatoid arthritis of the knee, flexion deformity may be prevented and pain lessened by the use of a posterior splint worn almost constantly while the patient is in bed (fig. 16). This splint should be removed at least once every twenty-four hours to allow guided or active motion through as full a range as possible to prevent adhesions. This is most effective following the use of hot fomentations.

Flexion deformities may be corrected by the application of solid plaster leg casts applied in the position of maximum correction and kept on for forty-eight hours. These should then be bivalved and removed, and the joints moved through as full a range of motion as possible. The posterior half of the bivalved casts are used as resting shells. Seventy-two hours should elapse before further correction is attempted. In the interim daily heat, massage and active or guided motion may be carried out. Balanced traction, the hinged cast method and the use of wedged cylinders or Turner irons may all be valuable at times in correcting such deformities. When maximum correction has been gained by any of the methods mentioned, a caliper splint (fig. 17) may be fitted to retain the extension gained or even to secure further corrections. This method allows the patient to be ambulatory.

Fig. 20.—Foot supported by spring steel arch support covered with thin leather.

After correction has been attained for a bedridden patient and weight bearing is ready to be started, the knee joint must be carefully protected and supported because of the weakness of the quadriceps muscles and other periarticular structures. For the more severe cases, a rigid cylinder, with a hole for the patella (fig. 18) may be used to support the joint during weight bearing until the quadriceps muscles are strong enough. For the simpler cases with good quadriceps muscles an elastic bandage with a felt strip on either side of the patella will give adequate support. Daily use of elastic overhead traction,[12] "knee-push" apparatus (fig. 19) or heat and massage to tone up weakened and atrophied muscles constitute further aids in rehabilitation. A step further in this direction would be the use of occupational therapeutic devices, such as the treadles on looms and the pedals on jig saws.

Fig. 21.—Figure of eight ankle straps.

FEET

The arthritic patient who possesses a foot under constant strain finds it less resistant to the disease.[15] A foot with well protected arches is not so likely to be attacked. Furthermore, if deformities are present at either the hip or the knee there may be a resulting foot strain. For example, permanent flexion of the knee may produce a sufficient strain on the metatarsal heads to produce acute pain. External rotation of the leg leads

14. Smith-Petersen, M. N.: Arthroplasty of the Hip—A New Method, J. Bone & Joint Surg. **21**: 269 (April) 1939.

15. Kuhns, J. G., and Swaim, L. T.: The Prevention of Deformities in Chronic Arthritis, J. A. M. A. **93**: 1853 (Dec. 14) 1929, **94**: 1123 (April 12) 1930 and **94**: 1743 (May 31) 1930.

to pronation or longitudinal arch strain. When a patient has been confined to bed for a long time the muscles and ligaments become relaxed and foot strain appears on weight bearing. In all such instances the feet must be well protected by arch supports (fig. 20) and strengthened by exercises. Foot hygiene must be just as carefully carried out in the arthritic as in the diabetic patient.

With the onset of arthritis in the ankle or tarsal joints, protective muscle spasm appears and tends to pull the foot into a valgus position. Furthermore, the pull of the gastrocnemius muscle, aided by the force of gravity and the weight of the bed clothes, tends to thrust the foot into an equinus position. This resultant equinovalgus deformity not only causes the front arch to be depressed during weight bearing but leads to a cocking-up of the toes as well. In time, so-called hammer toe deformities are present.

In the acute phase, when the feet are swollen and painful, weight bearing is definitely contraindicated. In such cases a plaster boot that extends from below the knee to just proximal to the metatarsal heads on the plantar surface and to the tips of the toes dorsally is usually worn with comfort. It must be bivalved so that the foot may be removed for daily motion or physical therapy. The bed clothing must be held off the feet, preferably by a cradle or by a pillow or a broad board

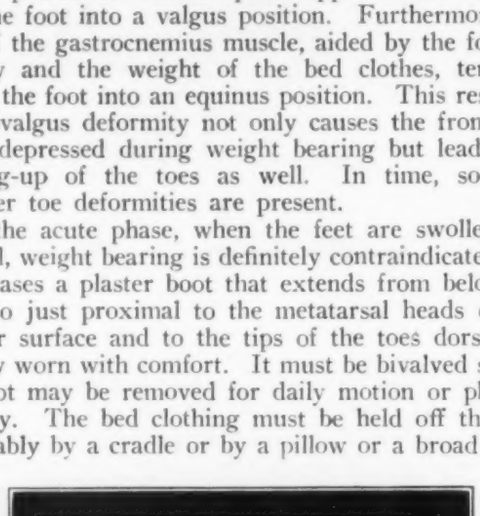

Fig. 22.—Anterior arch cuff made of soft leather.

placed at the foot of the bed. Foot exercises should be taught these patients as soon as the foot is pain free.

Weight bearing is allowed when swelling and pain have disappeared, provided the feet are equipped with good shoes and arch supports. So-called figure of eight walking straps (fig. 21) may give additional support to the longitudinal arch and prevent widening of the ankle mortise. Likewise the acute bursitis accompanying hallux valgus deformities may be prevented by a simple foot cuff (fig. 22) worn just proximal to the heads of the metatarsals.

If deformities have taken place, they may be corrected by serial plaster casts left on for forty-eight hours. These are then bivalved to permit motion and physical therapy. A new attempt at correction can then be made in seventy-two hours. Manipulations under anesthesia are helpful in gaining better positions, but these should be held in plaster for four to six days. In the most refractory cases operative measures, such as a fusion or a radical correction of hammer toes, may be resorted to.

Too much cannot be said about properly fitting shoes for any patient with foot disturbances, especially arthritis. The shoe should grip the longitudinal arch and possess sufficient width and length to avoid crowding the toes. In women's shoes it is important to have a wide base heel to prevent instability.

SUMMARY

Preventive and simple corrective measures are available for the treatment of arthritic joints. Flexion deformities can be prevented and joint motion maintained in a great proportion of the cases if early and persistent treatment is given. When deformities have occurred, corrective measures may be instituted with the assurance of some improvement. When fusion is inevitable the joint should be allowed to ankylose in the optimum functional position.

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THE PREVALENCE OF MALNUTRITION

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Recent estimates of the prevalence of malnutrition in the United States have varied so greatly that the Food and Nutrition Board of the National Research Council has assigned to us, as a subcommittee, the task of evaluating existing evidence on this question. Among the reasons for the widely varying estimates is the lack of criteria for the diagnosis of malnutrition. It is therefore necessary before discussion of the evidence that terms be defined.

DEFINITIONS

"Nutritional failure" exists as soon as adequate amounts of an essential nutritional factor or factors fail to reach the "milieu interne."

"Dietary inadequacy" means the failure to ingest an essential nutritional factor or factors in amounts sufficient to meet the existing requirement of the body.

"Nutritional inadequacy" means not only the failure to ingest, i. e. dietary inadequacy, but failure to absorb, to retain and to utilize an essential nutritional factor or factors in amounts sufficient to meet the existing requirements of the body.

"Malnutrition" is a bodily condition, detectable by any method of examination, caused by a nutritional inadequacy.

Nutritional Failure

Nutritional inadequacy May be caused by:	→ Malnutrition The successive stages of which are:
1. Dietary inadequacy	1. Tissue depletion
2. Failure to absorb	2. Biochemical "lesions"
3. Failure to utilize	3. Functional changes
4. Hastened excretion	4. Anatomic lesions

In accordance with these definitions, nutritional failure consists not only of disease entities sufficiently advanced to cause the florid manifestations of malnutrition such as pellagra, beriberi, scurvy, rickets and ophthalmia, but any stage of a sequence or chain of events as illustrated in the tabulation. The first link in the chain is nutritional inadequacy followed after variable periods of time by malnutrition, the successive stages of which

From the Food and Nutrition Board of the National Research Council, Washington, D. C.

are tissue depletion, biochemical "lesions," functional changes and finally anatomic lesions.[1]

The evidence on the prevalence of malnutrition is of three kinds: (1) food consumption records or dietary surveys, (2) official death rates and hospital admission figures, and (3) medical assessments of the nutritional status in samples of the population. These three methods should not be expected to yield identical information. Even when each is as fully developed and as accurately interpreted as possible, the result can only show trends reasonably parallel.

EVIDENCE FROM FOOD CONSUMPTION RECORDS AND DIETARY SURVEYS

Studies of food consumption do not show directly the nutritional status as a body condition, i. e. malnutrition, but they do show what proportion of families in the sample of population studied have a dietary inadequacy. These studies relate directly to this first link, while the most precise method of diagnosing malnutrition relates to some later link. The yardsticks or criteria adopted for an adequate diet influence the apparent incidence of dietary inadequacy. If the criteria adopted are such that the diets will just support life, then the figure expressing the apparent incidence of inadequate diets will be minimal. If the criteria adopted for an adequate diet are such as will prevent malnutrition under ordinary physiologic conditions, the apparent incidence of inadequate diets will be larger. If the criteria are such as will promote optimal health and well being, the number of apparently inadequate diets recorded will be largest.

The Bureau of Home Economics of the Department of Agriculture,[2] for example, has food consumption records of over two thousand families of wage earners, clerical workers and nonrelief, nonsharecropper farm families from all sections of this country. This survey found that 43.6 per cent of these families (59.5 per cent city, 16.3 per cent farm) failed to receive a "fair" [3] diet, and 76.2 per cent (92.1 per cent city, 49.0 per cent farm) failed to receive a "good" [4] diet. Unfortunately the Bureau of Home Economics has not yet published the incidence of diets failing to reach the Recommended Daily Allowances for Specific Nutrients [5] adopted by the Committee on Food and Nutrition of the National Research Council and approved by the Council on Foods and Nutrition of the American Medical Association.[6] These recommended allowances are not significantly different from the Bureau of Home Economics standards for a "good" diet, except that the allowances of thiamine and riboflavin are higher. This newer yardstick would probably increase the number in the group not obtaining a satisfactory diet.

In evaluating this dietary survey it should be pointed out that the records of food consumed were based on food entering the home and did not take into account waste, cooking losses (which may be very high for ascorbic acid and thiamine) or food (other than meals) and beverages purchased and consumed away from home. The first two unaccounted factors would tend to decrease the actual intake of the specific nutrients as against the recorded intake. The latter factor in some instances would add significantly to the nutritive quality of the diets, while in other instances the consumption of vitamin-free foods such as candy and carbonated and alcoholic beverages would depress the nutritive quality of the diets. It should also be pointed out that this survey did not include unemployed persons on relief, WPA workers, sharecropper farm families or high income families. While it may be imprudent to accept surveys of but few more than two thousand families, however well selected by sound sampling procedures, as representative of nearly thirty-five million families,[7] it should be pointed out that all surveys, whether conducted by private or by governmental agencies, both in the United States and Canada, are in general agreement that there is a high proportion of poor diets among the employed population.

EVIDENCE OF OFFICIAL MORTALITY RATES

Evidence based on official mortality rates (table 1) at best can furnish only information on the prevalence of the terminal link in the chain of nutritional failure, i. e. anatomic lesions; and of these only the irreversible, or rather the unreversed, appear since they represent in many instances therapeutic failures in recognized cases. These rates as published, however, do not furnish a reliable index even of deaths from malnutrition. This is due in part to nonrecognition of these and of other nutritional factors causing death, in part to mislabeling and in part to the statistical practice of giving precedence to certain diseases as causes of death over others. It would be interesting to know how much malnutrition is concealed in the 370,600 deaths recorded in 1938 under the heading "diseases of the circulatory system" or in the 75,431 deaths entered under its subclassification "diseases of the heart, unspecified," or among the 2,569 deaths listed as due to "alcoholism" or to know how much is masked by the nomenclature of "senility," "cirrhosis of the liver" [8] and "psychoses." [9]

TABLE 1.—*Deaths from Various Causes in the United States Registration Area, 1933-1938*

Cause of Death	1938	1937	1936	1935	1934	1933
Pellagra	3,205	3,258	3,740	3,543	3,692	3,955
Beriberi	42	21	11	7	5	1
Scurvy	30	27	33	30	36	28
Rickets	244	235	270	261	292	339

Another important factor in evaluating this type of evidence is that the morbidity rates for malnutrition are

1. Jolliffe, Norman: Treatment of Neuropsychiatric Disorders with Vitamins, J. A. M. A. **117:** 1496 (Nov. 1) 1941.

2. Stiebeling, H. K., and Phipard, E. F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities, Circular 507, U. S. Dept. of Agriculture, 1939. Stiebeling, H. K.; Monroe, D.; Coons, C. M.; Phipard, E. F., and Clark, F.: Family Food Consumption and Dietary Levels, Misc. Pub. 405, U. S. Dept. of Agriculture, 1941. Stiebeling, H. K., and Coons, C. M.: Present Day Diets in the United States, in Food and Life, Yearbook of Agriculture, U. S. Dept. of Agriculture, Washington, D. C., 1939, table 3, p. 296.

3. The Bureau of Home Economics' standard for a "fair" diet for a standard person consisted of protein 45 Gm., calcium 0.45 Gm., phosphorus 0.88 Gm., iron 10 mg., vitamin A 3,000 international units, vitamin B_1 250 international units, ascorbic acid 37 mg. and riboflavin 0.9 mg.

4. The Bureau of Home Economics' standard for a "good" diet for a standard person consisted of protein 67 Gm., calcium 0.68 Gm., phosphorus 1.32 Gm., iron 15 mg., vitamin A 6,000 international units, vitamin B_1 500 international units, ascorbic acid 75 mg. and riboflavin 1.8 mg.

5. Recommended Allowances for Various Dietary Essentials, Committee on Food and Nutrition, National Research Council, J. Am. Diet. A. **17:** 565 (June-July) 1941.

6. Report of Council on Foods and Nutrition Dealing with the National Nutrition Conference for Defense, J. A. M. A. **116:** 2783 (June 21) 1941. Report of Reference Committee on Executive Session, ibid., p. 2796.

7. The 1940 census gives 34,861,625 occupied dwelling units, which we have taken as approximating the number of families.

8. Jolliffe, Norman, and Jellinek, E. M.: Vitamin Deficiencies and Liver Cirrhosis: Part VII. Cirrhosis of the Liver, Quart. J. Studies on Alcohol **2:** 544 (Dec.) 1941. Daft, F. S.; Sebrell, W. H., and Lillie, R. D.: Production and Apparent Prevention of a Dietary Liver Cirrhosis in Rats, Proc. Soc. Exper. Biol. & Med. **48:** 228 (Oct.) 1941. Diet and Cirrhosis of the Liver, Current Comment, J. A. M. A. **117:** 1542 (Nov. 1) 1941.

9. In the Medical Service of the Psychiatric Division of Bellevue Hospital alone, in a recent five year period, 94 deaths were recorded as "alcoholic encephalopathy" which we now know were due to nicotinic acid deficiency (Jolliffe, Norman; Bowman, K. M.; Rosenblum, L. A., and Fein, H. D.: Nicotinic Acid Deficiency Encephalopathy, J. A. M. A. **114:** 307 [Jan 27] 1940. These deaths entered the official mortality statistics under the heading of either "alcoholism" or "psychoses."

high in proportion to the mortality. For example, Goldberger and his associates [10] estimated on the basis of a survey in 1917 that there were at least 33 cases of pellagra for each death reported. Sebrell [11] has recently pointed out that this figure is too low, for at that time only pellagra with cutaneous manifestations was recognized. A further factor tending to decrease the ratio of mortality to morbidity in recent years is the improvement in methods of care. Independently, both Sydenstricker and Sebrell arrived at an estimate of 100,000 cases of active pellagra in the United States in 1938.[12]

It is therefore our opinion that the mortality rates published by the Bureau of Vital Statistics do not indicate the true death rate from classic deficiency diseases. Even the apparent rising incidence in death attributed to beriberi, from 1 in 1933 to 42 in 1938, suggests this; for it is unlikely that there has been a many-fold increase in fatal thiamine deficiency during this period, and the statistical increase must be ascribed to increasing recognition and better diagnosis. It is thus probable that deaths actually due to malnutrition are many times greater than the mortality statistics indicate.

TABLE 2.—*Gross Evidences of Malnutrition*

System	Finding	Suggested Deficiency or Syndrome	Reference
Eyes	Xerosis conjunctivae and cornea	Vitamin A	Kruse.[29] Jolliffe.[31]
	Central ophthalmoplegia	Thiamine	Jolliffe, Wortis and Fein: Arch. Neurol. & Psychiat. **46**: 569 (Oct.) 1941. Wortis, Bueding, Stein and Jolliffe: Pyruvic Acid Studies in Wernicke Syndrome, to be published.
Mucous membranes	Scarlet red stomatitis and glossitis with or without secondary Vincent's infection	Nicotinic acid	Spies, Vilter and Ashe.[32] Rosenblum and Jolliffe: J. A. M. A. **17**: 2245 (Dec. 27) 1941. King: Lancet **1**: 32 (July 13) 1940.
	Magenta glossitis	Riboflavin	Spies, Vilter and Ashe.[32] Sebrell: Ann. Int. Med. **15**: 953 (Dec.) 1941.
	Atrophic glossitis	Nicotinic acid, B complex, addisonian anemia, Plummer-Vincent syndrome	Spies, Vilter and Ashe.[32] Youmans.[25]
	Scorbutic gums	Ascorbic acid	Youmans.[25]
	Cheilosis	Riboflavin	Spies, Vilter and Ashe.[32] Sebrell and Butler: Pub. Health Rep. **53**: 2282 (Dec. 30) 1938. Jolliffe, Fein and Rosenblum: New England J. Med. **221**: 921 (Dec. 14) 1939.
	Nonspecific urethritis, balanitis, vaginitis	Nicotinic acid	Spies, Vilter and Ashe.[32]
Skin	Pellagrous dermatitis	Nicotinic acid	Spies, Vilter and Ashe.[32]
	Seborrheic lesions in nasolabial folds on face, behind ears and in skin folds	Riboflavin	Spies, Vilter and Ashe.[32] Jolliffe, Fein and Rosenblum: New England J. Med. **221**: 921 (Dec. 14) 1939. Sydenstricker.[32]
	Hyperkeratosis and hyperfolliculosis	Vitamin A	Youmans.[25]
	Hemorrhagic manifestations	Vitamin K, ascorbic acid	Butt and Snell: Vitamin K, W. B. Saunders Company, 1941. Youmans.[25] Ralli: Medicine **20**: 251 (Sept.) 1941.
	Fissures in angles of mouth	Riboflavin	Spies, Vilter and Ashe.[32] Sebrell and Butler: Pub. Health Rep. **53**: 2282 (Dec. 30) 1938. Jolliffe, Fein and Rosenblum: New England J. Med. **221**: 921 (Dec. 14) 1939. Sydenstricker.[32]
Neurologic	Characteristic bilateral symmetrical polyneuropathy	Thiamine	Spies, Vilter and Ashe.[32] Sebrell: Ann. Int. Med. **15**: 953 (Dec.) 1941. Jolliffe.[1] Strauss.[17] Jolliffe.[17] Jolliffe.[18]
	Combined system syndromes	Thiamine, B complex, addisonian anemia	Youmans.[25] Jolliffe.[18] Romano.[21] Sebrell: Ann. Int. Med. **15**: 953 (Dec.) 1941. Sydenstricker.[32] McLester: Nutrition and Diet in Health and Disease, ed. 3, W. B. Saunders Company, 1940.
	Wernicke's syndrome	Thiamine, B complex	Jolliffe, Wortis and Fein: Arch. Neurol. & Psychiat. **46**: 569 (Oct.) 1941.
	Nicotinic acid deficiency encephalopathy	Nicotinic acid	Jolliffe, Bowman, Rosenblum and Fein.[9]
	Progressive stupor and hebetude	Nicotinic acid	Cleckley, Sydenstricker and Geeslin: J. A. M. A. **112**: 2107 (May 27) 1939.
	Certain organic reaction psychoses	Nicotinic acid, thiamine and B complex	Cleckley, Sydenstricker and Geeslin: J. A. M. A. **112**: 2107 (May 27) 1939. Jolliffe, Bowman, Rosenblum and Fein.[9] Wortis and Jolliffe: New York State J. Med. **14**: 1461 (July 15) 1941. Jolliffe.[18]
Skeletal	Rachitic deformities and osteomalacia	Vitamin D, calcium, phosphorus	McLester: Nutrition and Diet in Health and Disease, ed. 3, W. B. Saunders Company, 1940. Youmans.[25] Hess.[24]
General	Underweight, underheight, edema, pallor	Calories, proteins, iron, B complex	McLester: Nutrition and Diet in Health and Disease, ed. 3, W. B. Saunders Company, 1940. Youmans.[25]

EVIDENCE FROM HOSPITAL ADMISSION RATES

Evidence based on hospital record room figures are subject to the same criticism as the official mortality rates, i. e. incompleteness due to nonrecognition, mislabeling and precedence given to certain diseases over others. In addition, two other factors make this index unreliable. The first is that the hospitalized population is not a representative group, for, like persons with the common cold, patients with malnutrition enter the hospital only when sequelae develop; on discharge neither the common cold nor malnutrition but only the sequelae appear as the discharge diagnoses. The second is that certain anatomic lesions of malnutrition may be so prevalent that they are disregarded. This is paralleled by the practice of recording other highly prevalent conditions. For example, in 1938, according to Bellevue Hospital records,[13] dental caries was recorded in only 0.68 per cent of its patients, whereas it is common knowledge that the incidence of dental caries in the adult population is near 90 per cent.

Recognition of vitamin deficiencies in hospital patients has recently been tabulated by questionnaires completed by the Massachusetts General Hospital, Johns Hopkins Hospital, County Hospital (Santa Barbara, Calif.), University of Kansas Hospitals and the Kansas City General Hospital, and published in THE JOURNAL.[14] In a combined total of 338,406 admissions to these hospitals (including 80,000 outpatients at the University of Kansas Hospitals), vitamin deficiency was recorded in but 483 cases, an incidence, we have calculated, of 1.43 per thousand admissions.

Figures from Bellevue Hospital, Boston City Hospital, Cincinnati General Hospital, Hillman Hospital and

10. Goldberger, Joseph; Wheeler, G. A.; Sydenstricker, Edgar, and King, W. I.: A Study of Endemic Pellagra in Some Cotton Mill Villages of South Carolina, Bull. 153, Hyg. Lab., U. S. P. H. S., 1929.
11. Sebrell, W. H.: Nutritional Diseases in the United States, J. A. M. A. **115**: 851 (Sept. 7) 1940.
12. Proc. Seventeenth Annual Conf. Milbank Memorial Fund, 1939.
13. Annual Report, Bellevue Hospital, 1938.
14. Clendening, Logan: The National Nutrition, Correspondence, J. A. M. A. **117**: 1035 (Sept. 20) 1941.

the university hospitals of Duke, Georgia and Vanderbilt would, we believe, have given a higher rate. For example, in 1938, of 35,813 patients [15] discharged from the general divisions of Bellevue Hospital [13] a specified vitamin deficiency was recognized in 197, or 5.5 per thousand. In addition, malnutrition due to deficiency of unspecified nutrients was recorded in 210 cases, a rate of 5.9 per thousand. Furthermore, there were 219 patients whose anemia was recorded as due to deficient intake of iron, a rate of 6.1 per thousand.[16] We thus have in Bellevue Hospital a recorded rate of malnutrition of 17.5 per thousand discharges. Even this figure includes only the most striking cases of malnutrition, for at Bellevue, as in other hospitals, most cases of malnutrition are not recorded. The prevalence of certain well recognized syndromes due to dietary inadequacy is greater in hospital patients than the total rate recorded by hospital record rooms. For example, the following groups of clinical states seldom if ever appear in record room pneumonia, advanced tuberculosis, delirium, ulcerative colitis, toxemias of pregnancy, gastrointestinal malignancy and liver cirrhosis is common. It is probable that these findings are usually observed and can be found recorded in the body of the hospital record. However, they seldom if ever appear in record room compilations.

The prevalence of nutritional polyneuropathy in patients having alcoholism, diabetes, pregnancy, gastrointestinal cancer, cirrhosis of the liver and long continued fevers is decidedly common but is customarily recorded as "alcoholic," "gestational," "diabetic," "cachectic," "infectious" or "toxic" "neuritis." [17] Cases with such manifestations of malnutrition are not included in the hospital rates as evidence of malnutrition. Another possibility is that the diagnosis of polyneuropathy is usually not made in the absence of foot and wrist drop, muscle atrophy and complete areflexia; yet it is recognized by numerous authorities that polyneuropathy can

TABLE 3.—*Prevalence of Secondary (Iron Deficiency) Anemia*

	Subjects	Criteria	Percentage Deficient		Reference
Ann Arbor	158 pregnant women (urban)	Hb. 10 Gm. per 100 cc. C.I. 0.9 C.Hb. 26 × 10-12 G	26.6		Bethall, Gardiner and Mackinnon: Ann. Int. Med. **13**: 91 (July) 1939.
New York City	(a) 325 pregnant women—iron therapy	R.B.C. 4,000,000	(a) 28		Labate: Am. J. Obst. & Gynec. **38**: 48 (July) 1939.
	(b) 307 pregnant women—no iron therapy	Hb. 11.6 Gm. per 100 cc.	(b) 72		
Oklahoma City	1,000 private obstetric patients	(a) R.B.C. 3,500,000 (b) Hb. 10.2 Gm. per 100 cc.	(a) 16.4 (b) 9.2		Eskridge and Serwer: South M. J. **32**: 24 (Jan.) 1939.
United States	Pregnant women (review)	"Iron deficiency anemia"	30-60		Gordon: Kentucky M. J. **38**: 415 (Sept.) 1940.
New York City	(a) 336 private school children	Boys, 13, and all girls, 12 Gm.	(a) 1.5		Wiehl: Milbank Memorial Fund Quart. **19**: 45 (Jan.) 1941.
	(b) 425 public school children	Boys, 13 yrs., 12.8 Gm. to 13.5 Gm.	(b) 3.3		Wiehl and Kruse.[39]
	(c) 138 WPA employees	Hb. 14 Gm. per 100 cc. Hb. 12 Gm. per 100 cc.	(c) 34 3.6		Wiehl and Kruse.[39]
Pennsylvania	428 school children (representative economic section)	Hb. 11.5 Gm. per 100 cc. Hb. 10.0 Gm. per 100 cc.	57 13		Zayas, Mack, Sprague and Bauman: Child Development **11**: 1 (Jan.) 1940.
Florida	620 rural school children (6-10 yrs.)	Hb. 11.7 Gm. per 100 cc. Hb. 9.6 Gm. per 100 cc. Hb. 11.7 Gm. per 100 cc. Hb. 9.6 Gm. per 100 cc.	85.2 57.2 77.4 33.4		Abbott and Ahmann: Am. J. Dis. Child. **58**: 811 (Oct.) 1939.
Pennsylvania	2,400, all ages		Male	Female	
	Preschool	Hb. 11.5 Gm. per 100 cc.	51	56	Mack, Smith, Logan, O'Brien, Shaw and Dodds: Milbank Memorial Fund Quart. **19**: 282 (July) 1941.
		Hb. 10.0 Gm. per 100 cc.	±20	±20	
	School	Hb. 11.5 Gm. per 100 cc.	14	26	
		Hb. 10.0 Gm. per 100 cc.	5	4	
	Adult	Hb. 11.5 Gm. per 100 cc.	20	30	
		Hb. 10.0 Gm. per 100 cc.	±15	±15	
New York City	100 hospital patients (medical)	Hb. 10.2 Gm. per 100 cc.	23		Scott and Janeway: New York State J. Med. **40**: 440 (March 15) 1940.

figures of malnutrition: hypoproteinemia; microcytic hypochromic anemia, macrocytic hyperchromic anemia; deficiency stomatitis and glossitis; nutritional polyneuropathy. The rate of malnutrition, if these groups were thus recorded on the discharge card, would be many times greater than 1.4 per thousand. It is true that increased excretion or failure of formation accounts for significant numbers of hypoproteinemias; that bleeding, infection and malignancy account for significant numbers of microcytic hypochromic anemias; that deficiency of the "intrinsic" factor and liver cirrhosis account for many macrocytic anemias; there remain, however, significant numbers of cases in which these findings can be explained only by dietary inadequacy of protein, iron, "extrinsic" factors or vitamins. The development of a scarlet red stomatitis or a glossitis due to a deficiency of nicotinic acid and of other B vitamins postoperatively and during such illnesses as express itself by only bilateral calf muscle tenderness, plantar dysesthesia, impaired vibratory sensation in the toes and absence of ankle jerks.[18] These criteria occurred in approximately 22 per cent of the alcoholic patients entering Bellevue Hospital,[19] in 17 per cent of those entering Boston Psychopathic Hospital [20] and in 30 per cent of those entering Colorado Psychopathic Hospital.[21] According to the same criteria, 2.1 per cent of ambulatory diabetic patients attending the Third Medical Division diabetic clinic at Bellevue Hospital [22] had a polyneuropathy which disappeared following the daily oral administration of 10 mg. of thiamine alone. It is thus obvious that much clinically evident malnutri-

15. The figures from the Psychiatric Division of Bellevue Hospital are omitted because these figures would include (1) the 12,000 alcoholic admissions, in which malnutrition is very prevalent and (2) the 3,000 admissions to the Medical Service of the Psychiatric Division, where the staff is actively interested in this problem.

16. This figure does not include macrocytic anemias, anemias due to poor food absorption, unknown cause, infections, blood loss, surgical conditions and prematurity, or anemias associated with blood dyscrasia.

17. Strauss, M. B.: Therapeutic Use of Vitamin B_1 in Polyneuritis and Cardiovascular Conditions: Clinical Indications, J. A. M. A. **110**: 953 (March 26) 1938. Jolliffe, Norman: A Clinical Evaluation of the Adequacy of Vitamin B_1 in the American Diet, Internat. Clin. **4**: 46 (Dec.) 1938.

18. Jolliffe, Norman: Clinical Aspects of Vitamin B Deficiencies, Minnesota Med. **23**: 542 (Aug.) 1940.

19. Jolliffe, Norman, and Goodhart, Robert: Beriberi in Alcohol Addicts, J. A. M. A. **111**: 380 (July 30) 1938.

20. Secunda, L., and Trowbridge, E. H.: Personal communication to the authors.

21. Romano, John: Deficiency Syndromes Associated with Chronic Alcoholism, Am. J. M. Sc. **194**: 645 (Nov.) 1937.

22. Fein, H. D.; Ralli, Elaine P., and Jolliffe, Norman: Peripheral Neuropathy Due to Vitamin B_1 Deficiency in Diabetes Mellitus, J. A. M. A **115**: 1973 (Dec. 7) 1940.

tion, if looked for, could have been detected without special technics.

The evidences of malnutrition of a gross nature that can be detected by a bedside examination without the aid of any laboratory technics have been listed in table 2, along with the deficiency which their presence suggests and references to the literature. It is implicit in their presentation that no single physical sign is necessarily diagnostic until evaluated in the light of other signs and symptoms, until other possible causes have been ruled out and the diagnosis confirmed. If these signs were routinely observed and recorded in all cases and their implications investigated, the apparent prevalence of malnutrition in hospital and office practice, simply by improved recognition, would probably be increased many times.

EVIDENCE FROM MEDICAL ASSESSMENT OF THE NUTRITIONAL STATUS OF POPULATION GROUPS

The evidence gathered by this procedure includes (1) the florid manifestations of deficiency diseases as represented by the classic syndromes of beriberi, pellagra, scurvy, rickets and ophthalmia, (2) the gross manifestations as listed in table 2 and (3) the subgross manifestations determined by special technic as listed in table 3. The procedures recommended in table 3 involve no equipment or chemicals not available in any well equipped hospital or clinic.[23]

TABLE 4.—*Special Examinations for Detection of Malnutrition*

Examination	Condition It May Detect
Roentgenogram of hand and wrist, elbow and hip	Rickets and scurvy in children; osteomalacia and scurvy in adults
Roentgenogram of heart	Advanced beriberi
Electrocardiogram	Changes suggestive of thiamine deficiency
Biomicroscopic eye examination with slit lamp	Capillary invasion of cornea (riboflavin deficiency); changes in conjunctivas (vitamin A deficiency)
Red blood cell count Hemoglobin Stained blood smear Red blood cell volume	Iron deficiency anemia; addisonian anemia; macrocytic anemia
Plasma ascorbic acid	Vitamin C undersaturation
Serum calcium Serum phosphatase Serum phosphorus	Vitamin D deficiency
Blood pyruvic acid	Vitamin B_1 deficiency
Serum protein or albumin	Protein deficiency
Blood prothrombin	Vitamin K deficiency

These special procedures are mostly for the detection of subgross anatomic manifestations. Only deficiency of protein, vitamin K and vitamin C may be detected by blood examination prior to development of anatomic lesions. Thiamine, nicotinic acid and vitamin A deficiency may be suspected on the basis of functional disturbances or chemical evidence, but a diagnosis cannot be made on the basis of such evidence alone. It is only by discovery of characteristic anatomic lesions that a diagnosis of rickets, osteomalacia or deficiency of iron, vitamin A, thiamine, riboflavin or nicotinic acid can be made. In some of these, biochemical changes are known to be present; but at the present time a diagnosis cannot with safety be based on chemical evidence alone. However, just as the development of special technics has led to earlier diagnosis of pregnancy, tuberculosis, malignant growths, heart disease and syphilis, so it is hoped that further developments of specialized technics will lead to the recognition of malnutrition before it has advanced to the stage of anatomic lesions.

It is obvious, therefore, that in the present state of our knowledge concerning the diagnosis of malnutrition due to many of the specific nutritional factors a wide borderline zone exists between nutritional inadequacy and diagnosable malnutrition. This borderline zone is often designated as "subclinical." As soon as a technic becomes available for the diagnosis of a manifestation it is no longer subclinical. The term "subclinical" has also been used to designate recognizable anatomic malnutrition that is subgross, such as capillary invasion of the cornea and some conditions that do not seem to be critical, such as cheilosis and mild rickets. This use is obviously incorrect, for these lesions are clinical and need only to be looked for to be found. In addition, the term has been used both as a cloak for ignorance and as a keynote for derision. For these reasons it should be dropped.

Data based on surveys which include examinations of populations for evidence of malnutrition are only now beginning to appear and are necessarily far from complete. Studies now under way, such as the cooperative studies by the Milbank Memorial Fund in New York City and in workers in defense industries elsewhere; and those under the auspices of the Rockefeller Foundation in North Carolina, Tennessee and Canada have been reported only in preliminary notes.

IRON DEFICIENCY ANEMIA

Statistics on the prevalence of iron deficiency (hypochromic) anemia in the American population are not nearly as complete as the figures available for the British Isles. All surveys, however, show a notably high incidence, especially in children and pregnant women of the lower income groups. In table 4 are listed some of the more recent surveys, indicating findings of anemia in from 1.5 to 85 per cent of children, 3.6 to 30 per cent during adult life and 9 to 72 per cent in pregnancy. It is recognized that chronic blood loss, malignant conditions and possibly factors other than an inadequate intake of iron may result in hypochromic anemia. However, in studies of large groups, particularly of school children, it is probable that the prevalence of hypochromic anemia is a reasonably accurate index of a dietary inadequacy in iron.

THE PREVALENCE OF RICKETS

With the development of knowledge of the cause and prevention of this disease, the prevalence of severe rickets has been greatly reduced in recent years. Twenty years ago, except for regions blessed with more than average sunshine, the prevalence of clinically detectable rickets in infants was estimated by Hess [24] at about 75 per cent. Present figures indicate that the prevalence of active and healed clinical rickets is approximately 20 per cent of children of preschool age. This figure varies greatly from community to community, depending on urbanization, age, season of the year, race and the practice of preventive treatment.[25] In Newark, N. J., Levy and Silver [26] studied, in the spring of 1937, 100 consecutive infants less than 9 months of age and

23. Certain tests have been omitted from this list for various reasons. Thus, methods for measuring dark adaptation such as the biophotometer and the adaptometer, although apparently reliable in the hands of competent observers [20] and with intelligent cooperative subjects, are dependent on subjective responses. Methods for blood vitamin A, riboflavin and thiamine are not included because satisfactory methods or criteria for their interpretation seem not to have been established. The same applies to urinary excretion studies of thiamine, riboflavin and nicotinic acid.

24. Hess, A. F.: Rickets Including Osteomalacia and Tetany, Philadelphia, Lea & Febiger, 1929.

25. Youmans, J. B.: Nutritional Deficiencies, Philadelphia, J. B. Lippincott Company, 1941.

26. Levy, Julius, and Silver, H. B.: Can Rickets Be Eliminated from a Large City? Arch. Pediat. **56**: 96 (Feb.) 1939.

found clinical evidence of rickets in 37 per cent. In North Dakota the state health department [27] reported in 1937 a study of 5,227 preschool children in whom by clinical methods active or healed rickets was found in approximately 20 per cent. In 1941 Rhoads and her co-workers [28] reported a study of 233 children at 2 years of age who had received 110 to 1,500 international units of vitamin D daily for the previous twenty-two months of life; active rickets was found in 7.7 per cent and healed rickets in an additional 6 per cent.

VITAMIN A DEFICIENCY

Reliable methods for the detection of early signs of vitamin A deficiency have not been available. However, Kruse [29] has recently shown that xerosis conjunctivae is a lesion which responds to the oral administration of large amounts of vitamin A. Wiehl and Kruse [30] then showed that 86.6 per cent of 494 pupils in a public school group and all but 1 of 143 WPA employees had some degree of xerosis conjunctivae. In 7.7 per cent of the public school group and in 45.5 per cent of the WPA group the xerosis conjunctivae was sufficiently advanced to form what the authors diagnosed as Bitot's spots, a condition long suspected as due to vitamin A deficiency.

In the wards of the Psychiatric Division of Bellevue Hospital, xerosis conjunctivae of a degree sufficient to form conjunctival elevations detectable with the unaided eye occurs in about 60 per cent of all patients.[31] The prevalence of these changes is greater among Negroes than among white persons, in male than in female, and in old than in young patients. If it is eventually confirmed that these or a portion of these changes in the conjunctivas are due to vitamin A deficiency it will be probable that the prevalence of this deficiency is many times that heretofore believed.

RIBOFLAVIN DEFICIENCY

Though ariboflavinosis is probably the most prevalent of the gross anatomic manifestations of B complex deficiencies [32] there are practically no medical surveys to indicate its frequency in the general population except the one recently reported by Wiehl and Kruse.[30] In this study evidence of riboflavin deficiency, in the form of characteristic vascular invasion of the cornea, was found in 2.3 per cent of the private school group, 75.8 per cent of the public school group and 38.4 per cent of the WPA personnel.

TABLE 5.—*Prevalence of Ascorbic Acid Depletion*

Place	Subjects—Vitamin C	Criteria	Percentage Deficient	Reference
			Autumn Spring	
Maine	86 school children	<0.6 mg. per 100 cc. serum ascorbic acid	69 85	Crane and Woods: New England J. Med. **224**: 505 (March 20) 1941
		<0.4 mg. per 100 cc. serum ascorbic acid	46 63	
			Summer Spring	
Tennessee	380 "normal" children	<0.7 mg. per 100 cc. serum ascorbic acid	45 61	Minot, Dodd, Keller and Frank: J. Pediat. **16**: 717 (June) 1940
Cincinnati	69 orphanage children	<0.5 mg. per 100 cc. serum ascorbic acid	15.9	Holmes, Cullen and Nelson: J. Pediat. **18**: 300 (March) 1941
		<0.25 mg. per 100 cc. serum ascorbic acid	5.8	
New York City	(a) 342 private school children	<0.6 mg. per 100 cc. serum ascorbic acid	(a) 5.5	Wiehl: Milbank Memorial Fund Quart. **19**: 45 (Jan.) 1941
		<0.4 mg. per 100 cc. serum ascorbic acid	2.9	
	(b) 425 public school children	<0.6 mg. per 100 cc. serum ascorbic acid	(b) 49.9	Wiehl and Kruse [30]
		<0.4 mg. per 100 cc. serum ascorbic acid	32.0	
	(c) 165 WPA employees	<0.6 mg. per 100 cc. serum ascorbic acid	(c) 55.2	Wiehl and Kruse [30]
		<0.4 mg. per 100 cc. serum ascorbic acid	39.4	
Washington Montana Oregon Utah Massachusetts Rhode Island	College students College students College students College students College students College students	<20 mg. daily urine ascorbic acid excretion	30-35 70 86	Fincke: J. Am. Dietet. A. **16**: 325 (April) 1940
Tennessee	900 rural population	(None given)	±20	Youmans: Am. J. Pub. Health **31**: 704 (July) 1941
North Carolina	218 persons, rural mill community	0 mg. per 100 cc. serum ascorbic acid	27	Milam and Wilkins: Am. J. Trop. Med. **21**: 487 (May) 1941
		<0.3 mg. per 100 cc. serum ascorbic acid	61	
California	70 hospital patients (surgical)	<0.5 mg. per 100 cc. serum ascorbic acid	77.1	Holman: Surg., Gynec. & Obst. **70**: 261 (Feb. 15) 1940
		<0.3 mg. per 100 cc. serum ascorbic acid	56.9	
		<0.15 mg. per 100 cc. serum ascorbic acid	12.9	
New York City	100 hospital patients (medical)	<0.7 mg. per 100 cc. serum ascorbic acid	33	Scott and Janeway: New York State J. Med. **40**: 440 (March 15) 1940
Chicago	100 hospital patients (unspecified)	<0.4 mg. per 100 cc. serum ascorbic acid	38	Croft and Snorf: Am. J. M. Sc. **198**: 403 (Sept.) 1939
		<0.3 mg. per 100 cc. serum ascorbic acid	19	
		<0.2 mg. per 100 cc. serum ascorbic acid	3	
New York City	157 hospital patients (medical)	<0.4 mg. per 100 cc. serum ascorbic acid	42	Jolliffe [31]

VITAMIN C UNDERSATURATION

Now that reliable methods are available for the determination of ascorbic acid in the blood, reports of the prevalence of vitamin C undersaturation in population groups are beginning to appear. This test represents the link of tissue depletion (as reflected in the blood) in the chain of events constituting nutritional failure and precedes the development of spongy gums and periosteal and subcutaneous hemorrhages by a considerable period of time. Just as a fasting blood sugar of 130 mg. per hundred cubic centimeters may not necessarily indicate the existence of diabetes mellitus, so the presence of fasting blood ascorbic acid level below 0.4 mg. per hundred cubic centimeters does not indicate scurvy, but both do indicate the necessity for dietary readjustment.

27. Orr, August: North Dakota State Health Department, cited by Woutat, P. H.: Journal-Lancet **58**: 493 (Nov.) 1938.

28. Rhoads, Teresa F.; Rapoport, Milton; Kennedy, Ruth, and Stokes, Joseph, Jr.: Studies on Growth and Development of Male Children Receiving Evaporated Milk: Effects of Various Vitamin Supplements on Growth and the Incidence of Rickets, J. Pediat. **19**: 169 (Aug.) 1941.

29. Kruse, H. D.: Medical Evaluation of Nutritional Status: IV. The Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes by Biomicroscopy, Pub. Health Rep. **56**: 1301 (July 27) 1941; Milbank Memorial Fund Quart. **19**: 207 (July) 1941.

30. Wiehl, D. G., and Kruse, H. D.: Prevalence of Deficiency Disease in Subclinical Stages, Milbank Memorial Fund Quart. **19**: 241 (July) 1941.

31. Jolliffe, Norman: Chapter on Nutrition and the Deficiency Diseases in Preventive Medicine in Modern Practice, New York, Harper & Brothers, to be published.

32. Spies, T. D.; Vilter, R. W., and Ashe, W. F.: Pellagra, Beriberi and Riboflavin Deficiency in Human Beings: Diagnosis and Treatment J. A. M. A. **113**: 931 (Sept. 2) 1939. Sydenstricker, V. P.: The Clinical Manifestations of Nicotinic Acid and Riboflavin Deficiency (Pellagra), Ann. Int. Med. **14**: 1499 (March) 1941. Sebrell,[13] Jolliffe,[14] Jolliffe.[31]

Williams and Wilder [33] have pointed out "that the normal organism in the basal state has remarkably constant levels of the various constituents of the blood, and that these levels are maintained until there is considerable depletion of stores or until there is disturbance of metabolism. Low levels of vitamins in the blood, therefore, may be evidences of severe rather than mild depletion of stores." As shown in table 5 there is evidence of vitamin C depletion (below 0.6 mg. per hundred cubic centimeters) in a large proportion of our population, ranging from 5.5 to 85 per cent of different groups.

Another method of study showing that the nutritional status of an important population group can be distinctly improved is that employed by Ebbs, Tisdall and Scott.[34] Exact records were taken of the food intake of women four months pregnant attending the antepartum clinic at Toronto General Hospital. The records were analyzed by the dietetic staff and a group was selected that had been consuming a poor diet containing approximately 1,600 to 1,900 calories, 60 Gm. of protein, 500 mg. of calcium and 10 mg. of iron. This group was then divided into two parts. No change was made in the diet of the first. Those in the second were furnished each day, as a supplement, one egg, 30 ounces of milk, ½ ounce of wheat germ, 1 ounce of cheese, 4½ ounces of canned tomatoes and one orange. This dietary improvement increased their calories to about 2,600, protein to 100 Gm., calcium to 1,600 mg. and iron to 24 mg. a day, besides materially raising the vitamin intake. The results are summarized in table 6. It should be noted that the "ratings" were made by an obstetric staff who did not know the dietary history of the patients. Even though, to be conservative, one might question the entire accuracy of these ratings, it is evident that a large number of these women and their children were materially benefited by

TABLE 6.—*Effects of a Poor and a Good Diet in 210 Pregnancies*

	Poor Diet	Supplemented Diet
Number of women	120	90
Obstetric antepartum rating "poor" or "bad"	36%	9%
Major complication during labor	47%	17%
Miscarriages and stillbirths	9.4%	0
Duration first stage of labor for primiparas	20.3 hrs.	15.2 hrs.
Condition during labor rated "poor" or "bad"	24%	3%
Condition during convalescence rated "poor" or "bad"	12%	4%
Final rating by obstetrician of whole course from fourth month through convalescence, "poor time" or "bad time"	34%	6%
Complication of mother during 6 months post delivery	46%	10%
Babies having poor or bad record first 2 weeks	14%	0
Number of babies who died under 6 months	3%	0

improvement in the diet and therefore that previously they had suffered in greater or less degree from nutritional failure. The results of these studies are important in indicating the prevalence of suboptimal nutrition in a population group—pregnant women—whose health is of special importance. They are even more significant, however, in demonstrating what may be achieved by better nutrition.

SUMMARY AND CONCLUSIONS

Malnutrition is accompanied by manifold signs and symptoms, diverse in nature, and to the casual observer their origin and significance are not always apparent. Some types of malnutrition are strikingly obvious to every one, some are apparent only to the physician who looks for them and some are vague and elusive even to the careful observer using the most accurate specialized technics. If the first group alone is counted the prevalence of malnutrition will be recorded as low, almost negligible. If the second group is counted it will be recorded as high. If the third group is included then the rate will be sufficiently high to occasion genuine concern.

The evidence at our disposal warrants the conclusion that dietary inadequacies and malnutrition of varying degrees are of frequent occurrence in the United States and that the nutritional status of an appreciable part of the population can be distinctly improved. If optimal nutrition is sought, not mere adequacy, then widespread improvement is possible.

39 East Seventy-Fifth Street, New York—930 South Twentieth Street, Birmingham, Ala.—Department of Chemistry, Columbia University, New York.

33. Williams, R. D., and Wilder, R. M.: The Prevalence of Malnutrition in the American Population: A Review of the Evidence, National Research Council Report, 1941.

34. Ebbs, J. H.; Tisdall, F. F., and Scott, W. H.: Influence of Prenatal Diet on the Mother and Child, J. Nutrition **22**: 515 (Nov.) 1941.

THE INFLUENCE OF SULFONAMIDE THERAPY ON POSTPNEUMONIC EMPYEMA THORACIS

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AND
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The dramatic beneficial effects of the sulfonamide derivatives in the treatment of pneumonia has naturally invited investigations concerning the effects of these drugs on empyema thoracis. There was even some hope that chemotherapy might largely eliminate the necessity of surgical intervention in cases of empyema by causing the disappearance of pus resulting from infections by organisms vulnerable to the sulfonamide derivatives. There is now, however, sufficient experience with postpneumonic empyemas in patients who had received adequate chemotherapy during the course of the pneumonia to state categorically that, once empyema thoracis (an abscess in the pleura) is present, adequate drainage of the abscess is essential. It becomes apparent, therefore, that the introduction of the sulfonamide derivatives has not altered in any way the fundamental principles of the management of empyema which were outlined by Graham and Bell [1] during the first world war. To add to the voluminous and exhaustive literature on the subject of empyema thoracis would hardly be justified were it not for the fact that sulfonamide therapy has so altered certain features of the clinical picture of empyema that it seems well to review our experiences with the disease since its use in the treatment of the pneumonias has become universal.

There is a large volume of literature treating many phases of the incidence and variables of postpneumonic empyema before the introduction of sulfanilamide, sulfapyridine and sulfathiazole. Howard [2] compiled some of the large reported series and found that empyema developed in 739 cases out of 24,730 cases of pneumonia, an incidence of approximately 3 per cent. Heffron,[3]

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1. Graham, E. A., and Bell, R. D.: Am. J. M. Sc. **156**: 839, 1918.

2. Howard, E. P.: The Diagnosis and Treatment of Pneumonia, New York, Oxford University Press, 1931, p. 373.

3. Heffron, Roderick: Pneumonia, New York, Oxford University Press, 1939, p. 1086.

in a compilation of 3,709 patients with pneumococcic pneumonia, most of whom were adults, found that empyema developed in 182, or 4.9 per cent. This author further analyzed the influence of the pneumococcic types on the incidence of empyema. Of 2,528 type I cases, empyema developed in 161, or 6.4 per cent. In 1,570 type II cases there was an incidence of 4 per cent. In 386 type III cases there were 17 cases of empyema, an incidence of 4.4 per cent. In group IV (old classification) there were 909 cases of pneumonia with 45 cases of empyema, or 5 per cent. Webster [4] has pointed out that yearly variations in the incidence of empyema can be correlated with similar yearly variations in type incidence. This variation likewise has been pointed out by Heuer.[5] Patterson [6] has found a definite seasonal variation in the incidence of empyema as a complication of pneumonia. That empyema occurs more frequently in the pneumococcic pneumonias of childhood is common knowledge. An incidence as high as 37.8 per cent has been reported by Lyon [7] in a series of type I pneumococcic childhood pneumonias. This is unusually high, of course. McCrae [8] and Heuer [5] agree that the severity of the pneumonia directly influences the incidence of empyema. The correlation between the virulence of the prevalent organism and the resulting empyema has been stressed by Graham and Berck.[9] Harloe,[10] analyzing 351 cases, found that the empyema was massive or generalized in 76.9 per cent, sacculated or interlobar in 18.6 per cent and bilocular in 2.3 per cent. It was bilateral in 2.3 per cent of the cases.

The dramatic results obtained in the therapy of the pneumonias with the sulfonamide compounds have led quite naturally to their universal use in these infections. While no such large series as cited in the presulfonamide era exists for comparative studies, the reported cases show a striking reduction in the incidence of empyema when the pneumonia has been treated with one of the therapeutically active sulfonamides. Hurwitz and Stephens [11] report an incidence of 0.9 per cent in 629 cases of pneumonia occurring in children. Schwartz and his collaborators [12] found an incidence of 2.3 per cent, and Flippin and his associates [13] found 5 cases out of 200. Wagoner and Hunting [14] saw only 1 case of empyema develop in 109 cases of pneumonia in infancy and childhood. Of these 55 developed in the sulfapyridine group. Carey,[15] in an analysis of 613 cases of pneumonia in children, found 20 cases of empyema. All of these 20 patients had pleural fluid when admitted to the hospital. In no instance did empyema develop after the institution of chemotherapy if fluid did not previously exist. Scott and Jones [16] saw empyema develop only once in 167 cases. Garvin,[17] in 40 cases of pneumococcic pneumonia treated with sulfathiazole, had but one complicating empyema, and in 62 cases treated with sulfapyridine saw only 4 cases. Thompson, Edwards and Hoagland [18] made comparative studies on the value of serum, sulfapyridine and the two combined during the winter of 1938-1939 in the St. Louis area. In a series of 121 cases of pneumococcic pneumonia treated with rabbit serum alone there were 12 cases of empyema. In another group of 142 cases treated with sulfapyridine alone there were only 4 cases. These same workers [19] had an opportunity to continue their studies on the 1939-1940 St. Louis series and present the striking fact that in 275 cases in which recovery occurred there was not a single case of empyema. Of these, 182 were treated with sulfapyridine alone.

Lanman and Heyl [20] were skeptical of the use of sulfonamides in empyema after pus had formed. These authors were impressed by the apparent change in the character of the exudate in the few cases they observed; they thought the pus was thicker and more tenacious.

Thus far the reports on the sulfonamide therapy of the pneumonias have been extremely vague for the most part, and in all instances very brief in their discussion of the complications. This is true with reference to the empyemas. It is difficult to get an accurate idea of the incidence of pleural complications and of their nature. Frequently pleural effusions have been mentioned with no further reference to their fate.

Before the introduction of sulfonamide therapy the clinical course of postpneumococcic empyema thoracis was in most instances very typical. Following the crisis of the pulmonary process there was an afebrile period of varying length followed by a sharp rise in temperature, which led to the discovery of an effusion. After a short time the effusion became frankly purulent and some form of drainage was instituted. If this was done promptly and adequately there was an immediate drop in temperature, the patient began to improve rapidly, and obliteration of the empyema pocket was complete in three to five weeks in almost all cases. The failure to obliterate pockets rapidly was unusual, and the necessity for secondary drainage operations was most infrequent.

To date we have had the opportunity to observe 30 cases of postpneumonic empyema which had been treated from the beginning of the illness with one of the sulfonamides. A considerably larger number have been treated, but on the remainder satisfactory data are lacking concerning the type and amount of drug administered. These cases occurred during the seasons of 1938-1939, 1939-1940 and 1940-1941. All ages are represented in the series. In all of the cases surgical drainage was instituted as soon as frank pus was obtained by thoracentesis. Patients in whom drainage had been delayed are not included because any peculiarity of localization of the empyema might result from the delay in evacuation of the pus.

The transition from effusion to frank pus was prolonged in the cases in which sulfonamide therapy was employed.

For comparative purposes a similar series of 29 cases of postpneumonic empyema not treated with any of the

4. Webster, R.: M. J. Australia **1:** 129, 1924.
5. Heuer, George J.: J. Thoracic Surg. **1:** 461, 1932.
6. Patterson, S. W.: M. J. Australia **2:** 115, 1922.
7. Lyon, A. B.: Bacteriologic Studies of 165 Cases of Pneumonia and Postpneumonic Empyema in Infants and Children, Am. J. Dis. Child. **23:** 72 (Jan.) 1922.
8. McCrae, Thomas: Bull. Johns Hopkins Hosp. **15:** 277, 1910.
9. Graham, E. A., and Berck, Maurice: Ann. Surg. **98:** 520, 1933.
10. Harloe, R. F.: Am. J. Surg. **26:** 231, 1934.
11. Hurwitz, Samuel, and Stephens, H. Brodie: J. Pediat. **14:** 11, 1939.
12. Schwartz, Louis; Flippin, H. F.; Turnbull, W. G., et al: Ann. Int. Med. **13:** 1000, 1939.
13. Flippin, H. F.; Schwartz, Louis; Rose, S. B., and others: Ann. Int. Med. **13:** 2038, 1940.
14. Wagoner, Stewart C., and Hunting, William F.: Sulfathiazole and Sulfapyridine, J. A. M. A. **116:** 267 (Jan. 25) 1941.
15. Carey, Benjamin W.: J. Pediat. **18:** 133, 1941.
16. Scott, John P., and Jones, Albert M.: J. Pediat. **17:** 423, 1940.
17. Garvin, Curtis F.: Comparison of Sulfathiazole and Sulfapyridine in Treatment of Pneumococcic Pneumonia, Arch. Int. Med. **66:** 1246 (Dec.) 1940.
18. Thompson, Lawrence D.; Edwards, Joseph C., and Hoagland, C. L.: Ann. Int. Med. **13:** 1138, 1940.
19. Thompson, Lawrence D.; Terry, Luther L., and Edwards, Joseph C.: J. Missouri M. A. **37:** 463, 1940.
20. Lanman, Thomas H., and Heyl, Henry H.: New England J. Med. **221:** 1003, 1939.

sulfonamides has been collected from our cases. This series likewise represents all age groups, and the cases have been taken in order without selection so that the two groups are comparable for statistical purposes. In the 29 cases of empyema reviewed here which were not treated by any of the sulfonamides all were general in type except 1, which was interlobar. Prompt recovery occurred in all, and in no instance was there any delay in obliteration of the pocket. In no instance was a secondary drainage operation required. In this group there were 23 pneumococcic cases, 7 type I, 9 group IV, 1 type III and 6 not typed. There were 5 hemolytic streptococcus cases, and in 1 case no growth was obtained.

In the sulfonamide treated group of 30 cases all ages are represented. Of the 30 cases 13 were treated with sulfapyridine, 10 with sulfathiazole, 3 with sulfanilamide, 1 with sulfamethylthiazole, 2 with sulfapyridine and sulfathiazole, and 1 with sulfathiazole and serum. Four cases were interlobar in type, 3 were encapsulated, 2 were posterior in type with an associated independent interlobar pockets and 1 was a small, encapsulated pocket in the vertebral gutter. In 9 of the cases there was marked delay in the reexpansion of the lung, and in 2 cases it was necessary to do secondary drainage operations. There were two deaths in this group, one due to a toxic hepatitis from sulfathiazole and one due to brain abscess. There were 25 pneumococcic cases, of which 11 were type I, 2 type III, 2 group IV (1 type V and 1 type XIX) and 10 not typed. There were 3 hemolytic streptococcus cases and 2 hemolytic staphylococcus cases.

While it is true that a relatively small series such as this represents does not warrant drawing too sweeping conclusions, yet the differences in the cases treated with sulfonamides are so striking as to be noteworthy. Furthermore, these differences are much more apparent to the experienced observer who actually follows the individual case than can be delineated by tables, graphs or descriptions. There is no denying the vast prognostic difference that sulfonamide therapy has wrought in the pneumococcic and streptococcic pneumonias. Neither is there any doubt that the treatment of the pneumonias with these agents has brought about a decided reduction in the incidence of complications, particularly empyema. From a presulfonamide incidence of approximately 5 per cent [21] the figure has been reduced to 1 per cent or less.[22] However, it is our belief that the picture of postpneumonic empyema has become so atypical and bizarre since the universal use of sulfonamide therapy in the pneumonias as to make a reevaluation of the disease necessary if we are to avoid committing grave errors in its treatment.

A consideration of the data presented demonstrates clearly the increased number of cases in which atypical empyema pockets occur. There is a much higher incidence of interlobar empyemas and a greater tendency to form either isolated or multiple encapsulated pockets which are difficult both of visualization and of adequate drainage. The number of cases in which reexpansion of the lung and obliteration of the pocket are delayed is disturbingly greater. Likewise the required number of thoracostomies for drainage in the individual case has increased.

21. Howard.[3] Heffron.[3]
22. Footnotes 11-19.

It is our belief that once the pneumonia has been adequately controlled, and certainly when pus has been demonstrated in the pleural cavity, sulfonamide therapy should be discontinued. To treat the empyema, once it has developed, chemotherapeutically is not only irrational but may be definitely deleterious. Such a course will only obscure the picture and render the proper surgical procedure more difficult. The idea, unfortunately too common among pediatricians and internists, that a purulent pleurisy caused by organisms affected by the sulfonamide drugs once formed will often take care of itself if chemotherapy is continued is just as fallacious as assuming that any other abscess will do the same without proper surgical drainage.

Two of the most valuable clinical guideposts in the proper treatment of empyema are the fever curve and the patient's appetite. In the case in which drainage has been adequate the temperature returns quite promptly to normal and the appetite becomes good and even voracious. Conversely, when for one reason or another the drainage becomes inadequate there is a prompt rise in temperature and an associated anorexia. The sulfonamides are notorious for their antipyretic properties and for their anorexic effects. The patient with a drained empyema who is being treated by one of these drugs often provides a confusing dilemma. One is lulled into a false sense of security by the antipyretic effect of the drug on the one hand and alarmed by its appetite destroying properties on the other.

It is to be hoped that, in the future, students of pneumonia will report their cases with more accurate data concerning the incidence and fate of the pleural complication.

Further studies on this problem are indicated so that the treatment of the pleural complications may remain rational. At present there is a real danger that the boon of sulfonamide therapy in the pneumonic patient may become a boomerang in the form of ill advised treatment of empyema.

SUMMARY AND CONCLUSIONS

1. A series of 30 cases of postpneumonic empyema thoracis occurring during or after sulfonamide treated pneumonias, together with a series of 29 cases which occurred in pneumonias not treated by any of the sulfonamide drugs, was studied.

2. A review of the literature makes apparent the reduction in the incidence of this complication since the introduction of sulfonamide therapy in the pneumonias.

3. Although the incidence is much less, we believe that the empyema when it does occur is very apt to be atypical and more difficult to treat satisfactorily. Though small, this series demonstrates differences far greater than can be explained by the many variables presented by the disease uninfluenced by sulfonamide therapy. There is a decided tendency to peculiar pocket formation with delayed reexpansion of the lung and obliteration of the empyema pocket. The number of secondary drainage operations is increased.

4. We feel that, once the pulmonary process is under control and pus has formed in the pleural space, sulfonamides should be discontinued.

5. Other series should be studied and reported in order that the therapy of the postpneumonic empyemas may remain rational and effective.

CHEMOTHERAPY IN THE MANAGEMENT OF LUDWIG'S ANGINA

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The condition now known as Ludwig's angina has interested surgeons for centuries. The frequency with which it is encountered depends to some extent on the definition of the entity one accepts. Most cases follow the extraction of a lower molar tooth. Hemolytic streptococci appear to be the most prevalent etiologic agents. Because of welling of the buccal contents, respiratory embarrassment is a common complication which at times may be severe enough to require tracheotomy. Mediastinitis and septicemia have also been noted.

The temperature in this condition varies widely and is not an indication of the severity of the process. Aside from the systemic symptoms which depend on the stage of the process and the presence or absence of those complications noted elsewhere, the clinical appearance is largely determined by swelling of the buccal contents. A hard, boardlike swelling externally may be limited at first to one side of the neck, corresponding to the location of the disease inside the mouth. This swelling usually extends to involve the neck in dog collar fashion. It is not fluctuant until late in the disease, since it is deep to the deep cervical fascia. The leukocyte count is usually moderately elevated.

Ludwig's angina should be differentiated from infections in the neck which are superficial to the deep cervical fascia and the mylohyoid diaphragm and from inflammatory processes intimately related to the lymphatics.

Treatment, as usually suggested, consists in wide incision and drainage. The use of sulfanilamide as an adjunct to surgical therapy has been suggested. A few cases have been reported recording recoveries after treatment with sulfanilamide in unmentioned dosage.

Mortality rates vary from 5 to 75 per cent, apparently mainly because different surgeons call different conditions Ludwig's angina. In Ludwig's 5 cases the mortality rate was 60 per cent.

CASES

I report 3 cases which seem to me properly to fall within the classification of Ludwig's angina. The report seems warranted because it was possible with the use of the sulfonamide drugs, particularly sulfathiazole, to bring about recovery without the aid of active surgical intervention. So far as I can determine, this has not previously been reported although, doubtless, other patients have been so treated.

CASE 1.—A white woman aged 32, admitted Jan. 6, 1941, had consulted a dentist because of an aching lower left second molar seven days previously. The tooth was extracted. Four days before admission the left side of the neck began to swell. Pain was not noted but the tumor was tender. At this time she complained of gradually increasing difficulty in opening her mouth, and swallowing became impossible. One day before admission the swelling extended across the midline anteriorly to the right side of the neck, and she felt feverish for the first time.

The patient was obese (192 pounds [87.1 Kg.], 5 feet 8½ inches [174 cm.]). On examination she did not appear acutely ill. There was no difficulty with respiration. The temperature by mouth was recorded as 102 F. The pulse was 104 beats a minute. Respirations averaged 24 a minute. The blood pressure was 150 systolic and 100 diastolic. The mouth could be opened 20 per cent of the normal range. The tongue was swollen and elevated and was protruding slightly. The bed of the left lower second molar was covered with a gray membrane which extended over the left side of the floor of the mouth. The floor of the mouth was greatly swollen, more on the left side than on the right side. Her breath was foul. There was a brawny, moderately tender swelling 8 cm. in diameter centering under the chin. Urinalysis showed the presence of albumin, graded 3 on the basis of 1 to 4, a few hyaline casts and a few cylindroids. The value for hemoglobin was not accurately determined and there were 4,680,000 erythrocytes and 15,000 leukocytes per cubic millimeter of blood. The differential blood smear revealed 8 per cent lymphocytes, 1 per cent monocytes, 1 per cent eosinophils and 90 per cent polymorphonuclears. The Kahn test for the presence of syphilis was negative. Staphylococci were cultured from material taken from the membrane covering the floor of the mouth.

Continuous moist warm dressings were applied to the neck and continuous steam inhalations were begun. A tracheotomy set was held in readiness. Fluids were supplied intravenously.

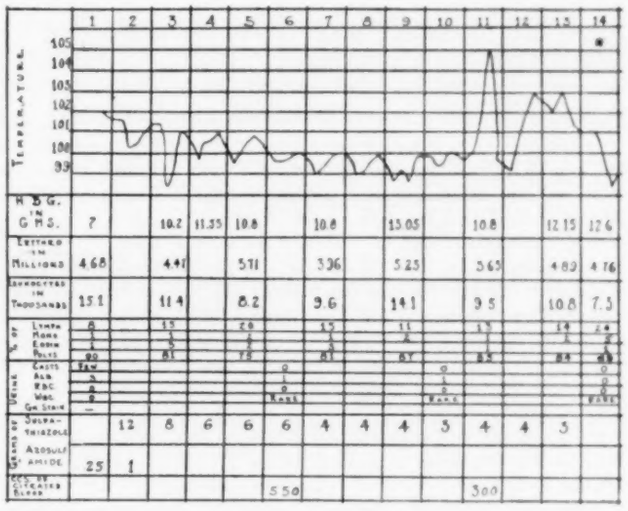

Chart 1.—Clinical course in case 1; * indicates that in the next four days the highest temperature was 99 F. and the patient was dismissed.

Five intramuscular injections of 5 cc. of 5 per cent azosulfamide were given in the first twenty-four hours. Sulfathiazole 120 grains (8 Gm.) was given rectally soon after admission, and within the next thirty-six hours an additional 120 grains of sulfathiazole was given by the same route in 60 grain (4 Gm.) doses.

The following day the patient could swallow and began to take fluid by mouth. She was given 15 grains (1 Gm.) of sulfathiazole every four hours. On January 9—three days after admission—she was able to take a soft diet. The swelling had decreased to about 75 per cent of its initial size. Reference to chart 1 will show that in four days the erythrocyte level fell about one million cells. Albumin and casts were disappearing from the urine and finally the urine became completely clear. She was given two transfusions, after the second of which she had a chill with a rise in temperature to 105 F. It is of interest that this patient's blood type IV failed to cross match with that of several type IV donors after she had been taking sulfathiazole for some time. By January 18 there remained but little swelling and the mouth could be opened normally; the temperature, however, was recorded as 103.8 F. by rectum. At this time a total of 64.3 Gm. (965 grains) of sulfathiazole had been given over a period of twelve days—an average of 5.36 Gm., or 80.4 grains, daily. Medication was discontinued and in twenty-four hours the temperature dropped to normal and in the next four days did not rise above 99 F.

From the Department of Surgery, the Gunning Clinic.

by rectum. The swelling had disappeared; the site of extraction of the left lower molar had completely healed and urinalysis was entirely negative. She was dismissed from the hospital, and subsequent check-up examinations have revealed no recurrence of the condition.

CASE 2.—A white man aged 58, admitted Feb. 5, 1941, had two days previously had the lower right lateral incisor extracted

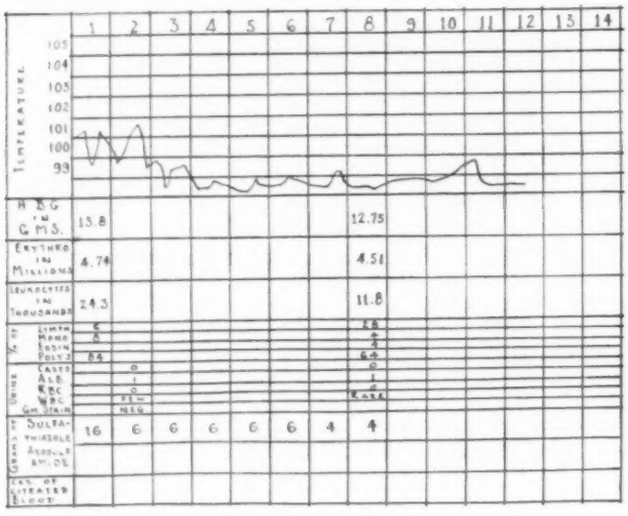

Chart 2.—Clinical course in case 2.

because of pain. One day before admission his neck began to swell on the right side and became painful. These symptoms increased, and on admission he was unable to swallow or expectorate, although he had no difficulty with respiration.

On examination the patient was well developed and well nourished and did not appear acutely ill. There was no difficulty with respiration. The temperature by mouth was recorded as 101 F., the pulse was 90 beats a minute and respirations averaged 22 a minute. The blood pressure was 140 systolic and 65 diastolic. The mouth could be opened quite widely. The tongue was swollen and elevated (grade 1 plus on the basis of 1 to 4). The bed of the right lower lateral incisor was edematous. The floor of the mouth was swollen (grade 1). There was a tender (grade 3) indurated swelling measuring about 8 cm. in diameter centering in the right submaxillary region. It was moderately firm, but one could not tell too much about this because of extreme tenderness. All remaining teeth were carious and very dirty. Gingival infection was extreme.

Urinalysis showed the presence of albumin (grade 1) and 3 to 4 plus cells per high power field in the centrifuged sediment. Gram stain of the sediment showed no organisms. The level of hemoglobin was 13.8 Gm. per hundred cubic centimeters of blood. There were 4,740,000 erythrocytes and 24,300 leukocytes per cubic millimeter of blood. The differential blood smear revealed 6 per cent lymphocytes, 8 per cent monocytes and 86 per cent polymorphonuclears. The Kahn test was not done. No material for culture was taken from the floor of the mouth.

The usual moist warm dressings and parenteral fluids were supplied. Mouth washes were used frequently. Owing to his inability to swallow, sulfathiazole was administered by rectum at first; 120 grains was given by this route at first, and this dose was repeated in twelve hours. The following day, February 6, the swelling had decreased slightly. The peak temperature was 101.6 F. by mouth. The patient was given 15 grains of sulfathiazole every four hours. By February 8, three days after admission, the temperature was normal (chart 2). On February 11, six days after admission, only a small firm area remained. The dosage of sulfathiazole was reduced to 60 grains daily. Reference to chart 2 will show that on February 12 the value for hemoglobin was 12.75 Gm. per hundred cubic centimeters of blood. There were 4,510,000 erythrocytes and 11,800 leukocytes per cubic millimeter of blood. The differential blood smear revealed 28 per cent lymphocytes, 4 per cent monocytes, 4 per cent eosinophils and 64 per cent polymorphonuclears. The urine showed a faint trace of albumin and a very occasional pus cell. The swelling was nearly gone on February 13. Sulfathiazole was discontinued. At this time the patient had taken, in eight days, 810 grains, or 54 Gm., of sulfathiazole, an average of 101.2 grains (6.75 Gm.) of the drug daily. During this time the fluid intake was never less than 2,500 cc. By February 15, ten days after admission, the swelling and soreness had disappeared completely. The patient was dismissed.

CASE 3.—A white boy aged 18 months was admitted Feb. 2, 1941. Two weeks previously his mother had noted sores on his lips which did not respond satisfactorily to various ointments. Two days before admission a swelling appeared in the right submaxillary and submental regions. The floor of the mouth became swollen. Trismus appeared and swallowing became impossible (this was a transient symptom). The family physician found the axillary temperature to be 103 F. and advised hospitalization.

On examination the patient appeared moderately ill. He was somewhat irritable. There was no difficulty with respiration. The rectal temperature was recorded as 104.2 F. The lower jaw could be moved through about three quarters of its normal range. The floor of the mouth was elevated (grade 1 plus) on the right. The tongue was not noticeably swollen. The throat appeared normal. The lips were dry and showed superficial encrusted lesions. A hard, moderately tender (grade 1 plus) swelling was present in the right submaxillary and submental areas. Urinalysis showed the presence of albumin (grade 1) and an occasional pus cell. The value for hemoglobin was 12.3 Gm. per hundred cubic centimeters of blood. There were 4,360,000 erythrocytes and 36,400 leukocytes per cubic millimeter of blood. The differential blood smear revealed 22 per cent lymphocytes, 5 per cent monocytes and 73 per cent polymorphonuclears. The Kahn test was not done. Culture of material swabbed from the floor of the mouth revealed hemolytic Staphylococcus aureus.

The general measures used in the previous 2 cases were employed. In the first thirty-six hours 30 cc. of 5 per cent azosulfamide was given intramuscularly, after which time the medication was changed. On February 4 he was given two 30 grain (2 Gm.) doses of sulfathiazole by rectum. On Febru-

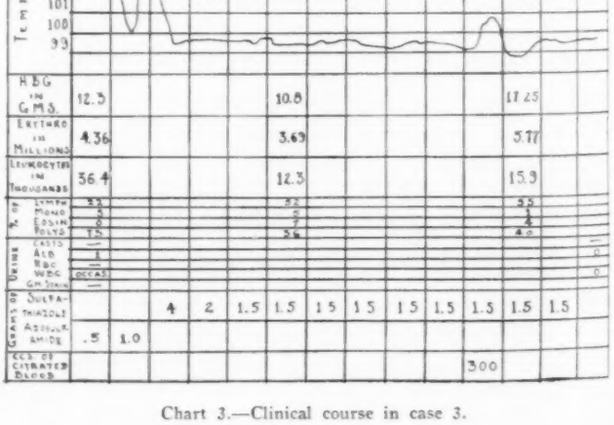

Chart 3.—Clinical course in case 3.

ary 5 he was given 30 grains of sulfathiazole by rectum. From February 6 to February 14 inclusive he received 7½ grains (0.5 Gm.) three times a day by mouth, making a total of 292½ grains (19.5 Gm.) of sulfathiazole in eleven days, an average of 26⅔ grains (1.77 Gm.) daily. The total dose of azosulfamide was 30 cc. of a 5 per cent solution (22½ grains equals 1.5 Gm.).

Reference to chart 3 will show that, with the exception of a transient rise in temperature to 100.8 F. rectally, on February 12, following a transfusion of 300 cc. of blood, his tempera-

ture did not deviate from the normal after the third hospital day. The child was given a transfusion because of a fall in the erythrocyte level to 3,690,000 from 4,360,000 within five days after admission. In the same length of time the leukocyte level had changed from 36,400 to 12,300 cells per cubic millimeter of blood, the blood smear at this time showing 52 per cent lymphocytes as compared with 22 per cent on admission and 36 per cent polymorphonuclears as compared with 73 per cent on admission. Urinalysis gave negative results after the course of medication was ended.

The swelling receded more slowly than in the other cases; a slight tumor remained when the child was dismissed on February 16, fourteen days after admission. The skin was freely movable over this swelling. It was not a gland and was situated deep to the mylohyoid diaphragm. The floor of the mouth was normal when the patient was dismissed. Follow-up examination, February 25, showed a barely perceptible area of induration and slight swelling where the tumor had been.

COMMENT

I do not wish to be understood as advocating the exclusive routine use of the sulfonamide drugs in the treatment of this malady regardless of the stage of disease or of the condition of the patient when he is first seen. Obviously, some will require immediate operation, either tracheotomy or wide incision or both, and preparations for such operations should always be made and held in readiness whenever a patient is admitted with a condition which may rather rapidly go on to produce respiratory embarrassment. However, in view of the experiences presented in this report, I do not see the necessity for precipitous surgery. It seems reasonable, in the absence of imperative indications for operation such as acute respiratory embarrassment or late fluctuation or continued severe constitutional disturbances, to treat these patients conservatively. I suggest that, so long as the term Ludwig's angina is apparently here to stay, when a patient presents an inflammatory process involving the floor of the mouth, deep to the mylohyoid diaphragm, as evidenced by elevation of the tongue, and producing a brawny induration of one or both submaxillary regions, with or without involvement of the submental region, which is obviously not confined within the lymphatics but bounded by tissue planes, he is to be considered as having Ludwig's angina.

Belief in the Common Man.—Democracy is a way of life controlled by a working faith in the possibilities of human nature. Belief in the common man is a familiar article in the democratic creed. That belief is without basis and significance save as it means faith in the potentialities of human nature as that nature is exhibited in every human being irrespective of race, color, sex, birth and family, of material or cultural wealth. This faith may be enacted in statutes, but it is only on paper unless it is put in force in the attitudes which human beings display to one another in all the incidents and relations of daily life. To denounce Naziism for intolerance, cruelty and stimulation of hatred amounts to fostering of insincerity if, in our personal relations to other persons, in our daily walk and conversation, we are moved by racial, color or other class prejudice; indeed, by anything save a generous belief in their possibilities as human beings and hence in the need of providing conditions which will enable these capacities to reach fulfilment. The democratic faith in human equality is belief that every human being, independent of the quantity or range of his personal endowment, has the right to equal opportunity with every other person for the development of whatever gifts he has.—Dewey, John: Creative Democracy—The Task Before Us, *Assn. Am. Coll. Bull.* **26**:198 (May) 1940.

FEBRILE REACTIONS ACCOMPANYING THE READMINISTRATION OF SULFATHIAZOLE

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Since sulfathiazole has been utilized frequently and successfully in the treatment of various infectious diseases, information concerning its undesirable reactions is of considerable importance.

It was observed that some patients who had been given one course of sulfathiazole without any deleterious effects had fever, often preceded by chills, shortly after the start of a second course of the drug.[1] The fever appeared to be associated with the administration of the sulfathiazole rather than with the infection for which the second course of the drug was given. When the sulfathiazole was discontinued, the fever subsided.

This type of reaction occurred in 36 per cent of the patients receiving a second course of the drug and is presumably due to a hypersensitivity to sulfathiazole.

METHODS AND RESULTS

Experiments on the Frequency and Time of the Febrile Reaction.—Fifty-three afebrile patients who received one course of sulfathiazole without complications were given a second course of the drug, usually for experimental purposes. Thirty-six of these patients received the initial course of sulfathiazole for therapeutic purposes for two to eighteen days (mean five and eight-tenths days) with clinical remission of their disease. Seventeen afebrile patients with no evidence of infection were considered controls and received the initial course of sulfathiazole for two days. The second course was started from two to twenty days (mean seven and eight-tenths days) after the completion of the first course.

A course of sulfathiazole consisted of an initial dose of 4 Gm. followed by 1 Gm. every four hours. The second course was given in exactly the same manner and continued for two to seven days unless a febrile reaction occurred.

Nineteen of the 53 patients (36 per cent) developed a severe febrile reaction with the administration of a second course of sulfathiazole. Eleven of the 36 patients (31 per cent) receiving the initial course for therapeutic purposes and 8 of the 17 controls (47 per cent) had a febrile response. This reaction occurred usually on the first day of the second course and was characterized by a sharp rise in temperature to between 102 and 106 F., accompanied frequently by chills. After the drug was discontinued the temperature returned to normal in from one to five days (mean two and nine-tenths days). Associated with the reaction there were profound prostration, weakness and exhaustion, often out of proportion to the temperature elevation and the general clinical condition, which persisted for several

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Work done by Dr. Balberor in partial fulfilment of the requirements for the degree of Master of Science in Medicine from Wayne University.

From the Medical Clinics of the William J. Seymour Division of Eloise Hospital, and the Departments of Medicine of the University of Michigan and Wayne University.

1. Lyons, R. H., and Balberor, Harry: Univ. Hosp. Bull., Ann Arbor **7**: 19-20 (March) 1941.

days after the fever subsided. Nausea, vomiting, delirium, stupor and conjunctivitis occasionally accompanied the pyrexic reaction. The details of the febrile reaction in these 19 cases are presented in the accompanying table.

Ten of the 19 patients experiencing a thermal response to a second course of sulfathiazole were given a third course in an attempt to reproduce the reaction. This third course was given in exactly the same manner as the preceding courses from ten to thirty-one days (mean seventeen days) after the termination of the previous febrile reaction. Eight of these 10 patients had the same type of reaction.

4 instances until between the ninth and the twelfth day after the first exposure to the drug. This was quite different from the immediate febrile reaction that was found when the second course was started ten or more days after the initial dose of sulfathiazole.

The interval between courses of the drug was prolonged to forty-one, thirty-five and thirty-three days respectively in 3 cases in which at least one febrile reaction had already been experienced. The readministration of sulfathiazole after these intervals was accompanied by a typical febrile response.

The effect of a single small dose of sulfathiazole was studied by administering doses varying from 0.25 Gm.

Cases in Which Two Courses of Sulfathiazole Were Administered with a Febrile Reaction to the Second Course

Case	Reason for Sulfathiazole Administration	Duration First Course, Days	Interval Between Courses, Days	Time of Reaction After Beginning Second, Hours	Amount of Drug Given Before Reaction, Gm.	Maximum Temperature	Chill	Days of Duration of Fever	Sulfathiazole Blood Level, Day of Reaction	Sulfathiazole Crystals in Urine	Eosinophils	Comment
S. M.	Lobar pneumonia.....	10	10	6	5	102	—	5	8.0	—	..	Moderate weakness and exhaustion
S. K.	Lobar pneumonia.....	3	9	15	7	104	+	1	1.7	—	..	Multiple chills, exhaustion and weakness
G. S.	Thrombophlebitis with infection	9	14	3	4	104	+	5	2.3	—	0	Severe exhaustion and weakness
E. R.	Bronchiectasis.....	9	10	4	5	102	+	4	...	—	12	Diffuse maculopapular dermatitis, nausea, vomiting
M. Y.	Cellulitis of face.....	9	8	4	5	103	+	1	...	—	..	Mild weakness
W. W.	Bronchopneumonia.....	5	7	10	9	104	—	3	10.0	—	..	Severe exhaustion and weakness
N. Z.	Lobar pneumonia.....	5	2	72	18	105	+	3	...	+	9	Severe exhaustion and weakness
T. G.	Pyelonephritis.....	4	9	4	4	104	+	2	...	..	..	Nausea, weakness and exhaustion
H. H.	Lobar pneumonia; acute epididymitis	7	10	12	7	104	—	3	3.5	—	0	Severe weakness and exhaustion
D. B.	Lobar pneumonia.....	6	5	12	7	102.4	—	5	4.4	+	0	Severe weakness and exhaustion
G. B. D.	Lobar pneumonia.....	5	4	16	8	102.4	+	1	4.3	—	2	Mild weakness
F. H.	Control.....	2	12	18	9	104	—	3	6.7	—	..	Nausea, vomiting, delirium, exhaustion and weakness
M. K.	Control.....	2	7	48	16	102	—	1	5.0	+	..	Mild weakness
E. C.	Control.....	2	7	18	8	104	—	4	8.0	+	1	Nausea, vomiting, severe weakness and exhaustion
J. W.	Control.....	2	2	216	57	103	—	3	3.7	+	8	Nausea and vomiting; severe weakness and exhaustion
Do. B.	Control.....	2	2	168	45	101	—	3	4.8	+	3	Mild weakness
P. P.	Control.....	2	4	48	15	103	+	1	5.5	—	0	Nausea and vomiting; weakness and exhaustion
F. Z.	Control.....	2	2	120	25	101.6	—	4	1.9	—	2	Mild weakness
A. S.	Control.....	2	7	16	9	104	—	2	2.5	—	..	Mild weakness

Subsequent full courses of sulfathiazole were given in 3 selected cases: two of these are described in detail in the case reports. The first patient received eight courses of sulfathiazole and after an uneventful initial course experienced seven distinct thermal reactions. In patients who experienced multiple febrile reactions, the later reactions tended to become less severe.

In an effort to determine the minimum time before a febrile reaction would develop with a second course of sulfathiazole, 8 controls were given a two day initial course of the drug. In 4 of these the second course was started after a two day interval and continued for eight days if no reaction occurred. In the other 4 a second course was started after a four day interval and continued for six days unless a fever developed. Two persons in each group experienced a febrile reaction during the second course of the drug. The time of onset of the fever, however, was delayed in these

to 1 Gm. to 7 patients who had previously experienced at least one febrile reaction. A 0.5 Gm. dose given to each of 5 patients produced a sharp febrile response in only 1 case. A 0.25 Gm. dose given to this patient three days later was without effect. When 1 Gm. of sulfathiazole was administered to each of 7 patients a mild thermal response was produced in 3. It was observed that following the repeated administration of small doses of sulfathiazole the reaction produced by a full course of the drug was diminished in intensity.

The hospital records of 200 consecutive patients receiving sulfathiazole were examined for the frequency of fever during a single course of the drug and for the duration of the sulfathiazole therapy. Only 5 patients (2.5 per cent) had fever attributable to the drug. In none of these cases was the fever experienced prior to the seventh day. Only 48 of the 200 patients received the drug for longer than seven days. Thus the

incidence of drug fever in cases in which the drug was administered for seven days or longer was 10.4 per cent.

Experiments on the Specificity of the Febrile Reaction.—Sulfanilamide and sulfapyridine were administered to each of 5 patients who had experienced febrile reactions following the readministration of sulfathiazole. The dose in each instance was 4 Gm. initially followed by 1 Gm. every four hours and continued for two to six days. However, these drugs failed to produce febrile reactions. Subsequent administration of sulfathiazole, given after the sulfanilamide or sulfapyridine, again produced the typical thermal response.

Experiments on the Possible Cause of the Febrile Reaction.—In general there was no change in the hemoglobin concentrations or total white blood cell counts during or after the febrile reactions. Differential blood counts done at the time of the febrile reaction showed no abnormalities except eosinophilia in 4 cases. In 1 case a diffuse maculopapular dermatitis accounted for the eosinophilia of 12 per cent, while in another there was a persistent eosinophilia before the second course was administered. In the other 2 cases the eosinophil counts of 8 and 9 per cent respectively are unexplained except by the possibility that the eosinophilia was due to the administration of sulfathiazole.

The serum bilirubin, icterus index and urinary urobilinogen determinations remained normal during the febrile reaction. There was no relation between the blood sulfathiazole concentration and the development of the fever. The concentration of the blood sulfathiazole at the time of the reaction varied from 1.7 to 10 mg. per hundred cubic centimeters.

Crystals of sulfathiazole were found in the urine in 6 of 19 cases (31.6 per cent) in which this type of reaction developed. However, since crystals were found in the urine in one third of the cases in which fever did not develop, little significance can be attached to this finding. There was likewise no difference in the incidence of microscopic hematuria. The administration of sodium bicarbonate in doses equal to the sulfathiazole did not prevent the febrile reaction.

Scratch and patch tests with sulfathiazole were negative in 5 cases in which thermal reactions had previously been experienced. Passive transfer studies were done by injecting 0.05 cc. of serum in these 5 cases into the skins of 15 normal persons. Scratch tests with sulfathiazole were performed on the area of skin so prepared twenty-four hours later in 10 cases and forty-eight hours later in the remaining 5 cases. These were all negative.

COMMENT

The high incidence of fever (36 per cent) associated with the readministration of sulfathiazole strongly suggests that the use of the drug is accompanied by more danger than was formerly considered. Not only is the patient exposed to the usual toxic effects of the drug and to the deposition of crystals in the urinary tract but also he may become predisposed to the development of a severe febrile reaction should it be necessary to repeat the drug at a later date. Therefore it is apparent that the use of sulfathiazole should be reserved for the more virulent and serious infections.

The incidence of fever during a single course of sulfathiazole was much lower than the 36 per cent that occurred with the second course. Reports on the incidence of sulfathiazole drug fever vary from 2 to 10 per cent.[2] In the 200 cases presented here in which one course of sulfathiazole was administered, only 5 experienced a febrile reaction, none occurring prior to the seventh day. This also corresponds with reports on other sulfonamide preparations which indicate that drug fever usually develops between the seventh and tenth days.[3] Since it is usually unnecessary to give sulfathiazole for longer than one week (76 per cent of the 200 patients in this series received the drug for less than seven days) the incidence of fever in the initial course can be expected to be low. If the patients receiving sulfathiazole for less than seven days are eliminated the incidence of drug fever in this series is 10.4 per cent.

It was observed that the few patients receiving a second course five to seven days after the initial exposure to the drug did not show a febrile reaction earlier than the ninth day. This finding suggests that a period of time elapses before this reaction can occur.

There is still a considerable discrepancy between the 36 per cent with febrile reactions when a second course of sulfathiazole is given and the 10.4 per cent of patients with drug fever occurring during a single course of seven or more days. This suggests that perhaps the presence of an interval between the courses of the drug predisposes more persons to a febrile reaction. It is well known that antigenic agents may often be administered continuously without any deleterious consequences, but, if an interval is interposed between courses of the antigen, hypersensitive reactions are more apt to occur. A similar hypothesis can be postulated to explain the greater incidence of fever when sulfathiazole is not administered continuously.

It is possible that sulfathiazole when introduced into the body may develop antigenic properties which in certain instances produce a state of hypersensitivity. The manifestation of this hypersensitivity in these cases is the febrile response. The fact that in the patients studied an interval of at least nine days was necessary between the first contact with the drug and the occurrence of a febrile reaction on readministration of the drug favors this assumption. Further evidence lies in the ability to reproduce the reaction repeatedly even after intervals of as long as forty-one days. Occasionally it is possible to produce such a high degree of hypersensitivity to the drug that very small doses may elicit a febrile response. If the sensitized person is given a succession of small doses, the febrile response to a full 4 Gm. dose apparently diminishes in severity. It is possible that small doses partially desensitize the patient to sulfathiazole. The relative specificity of the reaction also points toward the antigenic nature of the drug. Sulfapyridine and sulfanilamide were tolerated without difficulty when administered to patients who had exhibited at least one febrile reaction with sulfathiazole. Some patients, not in this series, however, have been seen who have developed fever with the administration of sulfathiazole after having had sulfa-

2. Spink, W. W., and Hansen, A. E.: Sulfathiazole, J. A. M. A. **115:** 840 (Sept. 7) 1940. Flippin, H. F.; Schwartz, Louis, and Rose, S. B.: Ann. Int. Med. **13:** 2038 (May) 1940. Flippin, H. F.; Rose, S. B.; Schwartz, Louis and Domm, A. H.: Am. J. M. Sc. **201:** 585 (April) 1941. Finland, Maxwell; Lowell, F. C., and Strauss, Elias: Ann. Int. Med. **14:** 1184 (Jan.) 1941. Callomon, V. B., and Goodpastor, W. E., ibid. **14:** 1024 (Dec.) 1940.

3. Council on Pharmacy and Chemistry: Sulfathiazole, J. A. M. A. **116:** 308 (Jan. 25) 1941. Lockwood, J. S.; Coburn, A. F., and Stokinger, H. E.: Studies on the Mechanism of the Action of Sulfanilamide, ibid. **111:** 2259 (Dec. 17) 1938. Keefer, C. S.: M. Clin. North America **23:** 1133 (Sept.) 1939.

pyridine or sulfanilamide. The demonstration of sensitivity to any drug by scratch, patch and passive transfer studies is in general exceptional; so the negative results do not necessarily rule out the hypothesis that this is a sensitivity reaction.

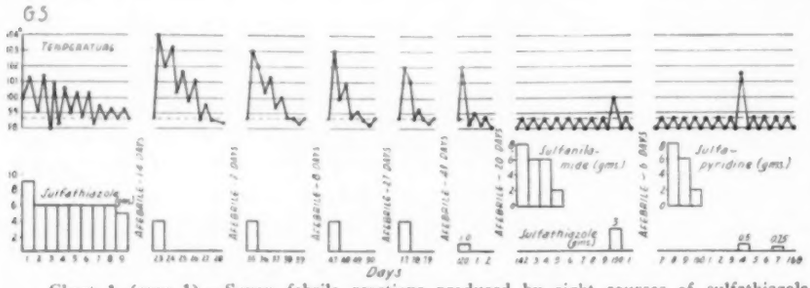

Chart 1 (case 1).—Seven febrile reactions produced by eight courses of sulfathiazole but no reaction with the final 0.25 Gm. dose. No reaction with sulfanilamide or sulfapyridine.

Other possible causes of the production of the febrile reactions have been considered and some at least can be eliminated. There is no evidence of a hemolytic crisis or other disturbance of the hemopoietic system. There is likewise no evidence suggesting involvement of the urinary tract as the cause of the reaction.

REPORT OF CASES

CASE 1.—G. S., a Negro aged 57, who had thrombophlebitis with cellulitis of the right leg, was treated with sulfathiazole for nine days until the temperature was normal and the cellulitis had regressed. After fourteen days with a normal temperature, 4 Gm. of sulfathiazole was administered for experimental purposes. Three hours later the patient had a severe chill, the temperature rose to 104 F., and weakness and exhaustion were noted. The fever gradually decreased over a period of five days after sulfathiazole was discontinued. A third course of sulfathiazole was started twelve days after the second course, the temperature having been normal for seven days. Two hours after the administration of 4 Gm. of sulfathiazole another pyrexic reaction developed. The temperature elevation persisted for three days. Twelve days later a fourth course was given consisting of 4 Gm. of sulfathiazole with 4 Gm. of sodium bicarbonate. Another reaction was experienced within two hours, and the fever persisted for two days. Thirty days later a fifth course consisting of a single dose of 4 Gm. of sulfathiazole and sodium bicarbonate was given, producing a reaction in three hours. Forty-one days later a single dose

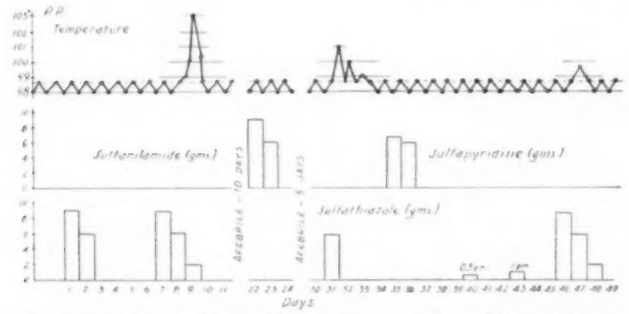

Chart 2 (case 2).—Three febrile reactions with sulfathiazole but no reaction with sulfanilamide or sulfapyridine or individual small doses of sulfathiazole. The first reaction to sulfathiazole occurred nine days after the initial exposure to the drug.

of 1 Gm. of sulfathiazole produced a typical reaction with temperature rising to 102 F. The temperature elevation persisted for only one day. After an afebrile interval of twenty days a four day course of sulfanilamide was uneventful. Four days later 1 Gm. of sulfathiazole was given every four hours for three doses and a temperature of 100 F. was observed. After six days without fever a three day course of sulfapyridine was given but no febrile reaction ensued. Five days later 0.5 Gm. of sulfathiazole produced the seventh thermal response, the maximum temperature elevation being 101.4 F. A still smaller dose of 0.25 Gm. of sulfathiazole failed to produce any reaction three days later. On no occasion was eosinophilia present in the peripheral blood or were sulfathiazole crystals present in the urine. Scratch and patch tests and passive transfer studies were negative.

CASE 2.—P. P., a white man aged 65, with bronchiectasis, was considered a control, since he was afebrile and improving for two weeks before the study was started. Sulfathiazole was administered for two days without any complications. Four days later sulfathiazole was started again and after he received 15 Gm. in forty-eight hours a severe chill was experienced and the temperature became elevated to 103 F. The patient experienced nausea and vomiting with severe weakness and exhaustion. Twenty-four hours after the drug was discontinued the temperature became normal. After a twelve day afebrile period sulfanilamide was administered for two days but no reaction occurred. Seven days later 4 Gm. of sulfathiazole was given and a temperature of 101 F. occurred within eight hours, returning to normal within two days. After two days with normal temperature, sulfapyridine was given for two days without a febrile reaction. Then 0.5 and 1.0 Gm. doses of sulfathiazole were administered on different occasions without producing fever. Finally a full course of sulfathiazole was administered over a three day period and a very mild temperature elevation ensued. The temperature rose to 99.6 F. and remained elevated for only one day. This suggests that a partial desensitization to the drug was produced by the preceding small doses.

SUMMARY

1. Nineteen of 53 patients (36 per cent) to whom sulfathiazole was readministered experienced a febrile reaction shortly after the beginning of the second course, although no fever attributable to the drug was experienced during the first course.

2. Febrile reactions were characterized by a sharp rise in temperature from 102 to 106 F. and were often accompanied by chills and associated with prostration and weakness.

3. Eight of 10 patients who had a thermal reaction with the second course experienced a similar reaction when given a third course of the drug. Certain selected patients had multiple febrile reactions when given repeated courses of sulfathiazole.

4. No patient exhibited a thermal reaction earlier than the ninth day, although the second course in some instances was started as early as the fifth day after the initial contact with the drug.

5. A febrile reaction occurred with the readministration of the drug, although the interval between courses was prolonged to as long as forty-one days.

6. In a series of 200 consecutive routine hospital cases in which a single course of sulfathiazole was administered, a drug fever developed in only 5. None of these occurred before the seventh day. If the cases in which the drug was given for less than seven days are eliminated, the incidence of drug fever in this series is 10.4 per cent.

7. It is suggested that the fever is due to a drug hypersensitivity and that the incidence of this reaction is enhanced by an interval between courses in contrast to the continuous administration of the drug.

8. The patients in this series who exhibited a thermal response to readministration of sulfathiazole were able to tolerate sulfanilamide or sulfapyridine without fever.

THE MISUSE OF SULFONAMIDE COMPOUNDS

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INDIANAPOLIS

With the general acceptance and use of the sulfonamide compounds, it is inevitable that they should be tried in many types of infections for which they are not considered specific. Such enthusiastic use is quite understandable because of the miracles chemotherapy has already brought to medicine.

It is not my purpose in this communication to question the experimental use of these drugs. It is my purpose to question certain pernicious surgical practices which seem to discard sound surgical judgment for the attractive mysticism of a newly found drug. These practices include (*a*) the "prophylactic" implantation of one of the sulfonamide drugs in a clean operative wound,[1] or any wound which is to be closed and (*b*) the local implantation of one of these drugs at the site of an appendectomy or appendical abscess.[2]

These practices have gained widespread popularity throughout the country as well as in our own community. There has been little inquiry into their rationale. The magic name of a sulfonamide compound has been sufficient authority to stuff it into every cavity, scratch, wound or orifice possessed by the human body. Some of these practices are logical, others are not. Two questionable practices are discussed here.

IN CLOSED WOUNDS

First of all it must be emphasized that sulfonamide drugs are quite irritant to the tissues. This is true of all the sulfonamides in common use. When placed in the tissues in powdered form, they cause an inflammatory reaction in those tissues.[3] The reaction may be

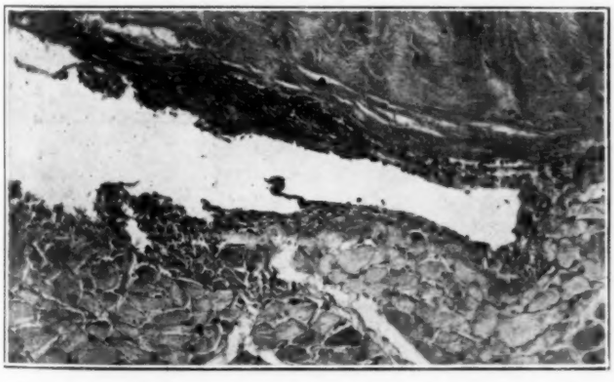

Fig. 1.—The illustrations show various inflammatory reactions produced by placing representative sulfonamide compounds beneath the anterior rectus sheath in the dog. Sections were taken after three days. This photomicrograph is a control, in which paraffin was placed beneath the rectus sheath. Paraffin has been dissolved out in the staining process, leaving an empty space. Note that there is practically no inflammatory reaction about this area.

moderate or it may be violent enough to cause the formation of an abscess.

In order to compare the irritant properties of these various drugs, a brief inquiry was undertaken. Approximately 1 grain (0.065 Gm.) quantities of common sulfonamides were placed beneath the anterior rectus sheath in the dog. The sheath was closed over the individual drug with a black silk suture and sections were removed three days later for microscopic study. Careful asepsis was maintained throughout the procedure. The powdered drug had been previously autoclaved. Drugs studied included sulfanilamide, sulfapyridine, sulfathiazole, sulfadiazine and sulfaguanidine.

It seemed desirable to have some type of control the better to evaluate the degree of irritation caused by these drugs. For this, small pieces of paraffin were

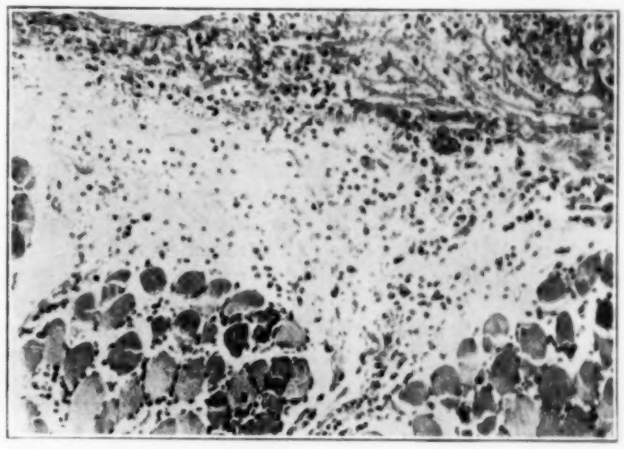

Fig. 2.—A similar area in which sulfanilamide has been placed. Note edema and moderate numbers of polymorphonuclears and monocytes.

buried beneath the rectus sheath and also sectioned for microscopic study after three days. Some paraffins are mildly irritant, but the one used produced practically no inflammatory reaction.

The results of this study were similar to those already reported.[4] Representative findings are reproduced in the illustration. All the drugs produced an inflammatory reaction with severe edema and accumulation of inflammatory cells. The latter consisted mostly of polymorphonuclears with moderate numbers of monocytes. In the case of sulfathiazole and sulfadiazine, actual abscesses were formed about crystals which still persisted in the tissues. No crystals remained at the end of the three day period in any of the other drugs (sulfanilamide, sulfapyridine and sulfaguanidine). Inflammatory changes were least in the case of sulfanilamide.

It is not within the scope of this study to discuss why some of the sulfonamides are more irritant than others. Possibly it is because the more soluble drugs are quickly absorbed and have less opportunity to irritate the tissues. This would seem to be at least partially true, since sulfanilamide is relatively soluble compared with sulfathiazole or sulfadiazine. The point is that all these drugs in the pure powder form are irritating to tissues—some to the point of being actually caustic.

Therefore, to place such an irritating substance in a clean wound would seem to be a questionable procedure. It undoubtedly damages and even kills cells with which it comes in contact. Such chemical trauma violates the fundamental principles of careful surgery and wound healing.

This criticism is not leveled at the local use of the sulfonamides on ulcers or contaminated wounds which are left open. Undoubtedly the drugs have a place in these situations, but in the present state of our knowl-

From the Departments of Surgery and Pathology, Indiana Universtiy School of Medicine.

1. Key, J. A., and Burford, T. H.: Prophylactic Implantation of Sulfanilamide in Clean Operative Wounds for Reduction of Postoperative Infections, Surg., Gynec. & Obst. **73:** 324 (Sept.) 1941. Diveley, R. L., and Harrington, P. R.: Chemotherapy in Infections of the Bones and Soft Tissues, J. A. M. A. **117:** 1868 (Nov. 29) 1941.

2. Jackson, H. C., and Coller, F. A.: The Use of Sulfanilamide in the Peritoneum, J. A. M. A. **118:** 194 (Jan. 17) 1942. Mueller, R. S., and Thompson, J. E.: Local Use of Powdered Sulfanilamide in Infections of the Peritoneal Cavity, ibid., p. 189. Long and Dees.[5]

3. Key, J. A.; Frankel, C. J., and Burford, T. H.: The Local Use of Sulfanilamide in Various Tissues, J. Bone & Joint Surg. **22:** 952 (Oct.) 1940. Throckmorton.[4]

4. Throckmorton, T. D.: The Peritoneal Response to Powdered Sulfonamide Compounds, Proc. Staff Meet., Mayo Clin. **16:** 423 (June 2) 1941.

edge it is certainly questionable that they should be sealed in any wound.

It is fully admitted that any drug which might be used locally as an antiseptic would be ideal if in so acting it did not damage the tissues more than the offending bacteria. Such a drug has not yet been demonstrated. At the present time it seems quite probable that such a drug will be developed in the future, but the present sulfonamides in powder form are most certainly not the answer.

A goodly number of enthusiastic reports are already in the literature singing the praises of sulfonamide powder implantation. It would seem that this testifies to the wonderful recuperative powers of human tissues under adverse circumstances rather than to the forethought of the operating surgeon.

IN APPENDICITIS AND APPENDICAL ABSCESS

During the past year a number of reports have appeared advocating the local use of sulfonamide drugs in cases of acute appendicitis or appendical abscess.[2] Several grams of the dry powder are placed in the peritoneal cavity presumably near the appendical focus. As much as 20 or 30 Gm. has been used in this manner.[5]

On first thought this would seem to be a logical procedure. It concentrates the drug in the local tissues far above that which might be reached by systemic administration. In fact the concentration reaches a point where the drug might be expected to exert a nonspecific effect as well as its expected action against specific organisms. What then are the objections to its use?

First of all, peritoneal adhesions may be expected if several grams of a powdered sulfonamide are placed in any one site. This is logical to assume, since it is well known that other irritants produce peritoneal adhesions and has already been demonstrated in animals.[4] Of course, this objection is not valid in the case of a walled off appendical abscess. On the other hand there seems to be no indication for implanting the drug in such a situation, since adequate drainage is sufficient.

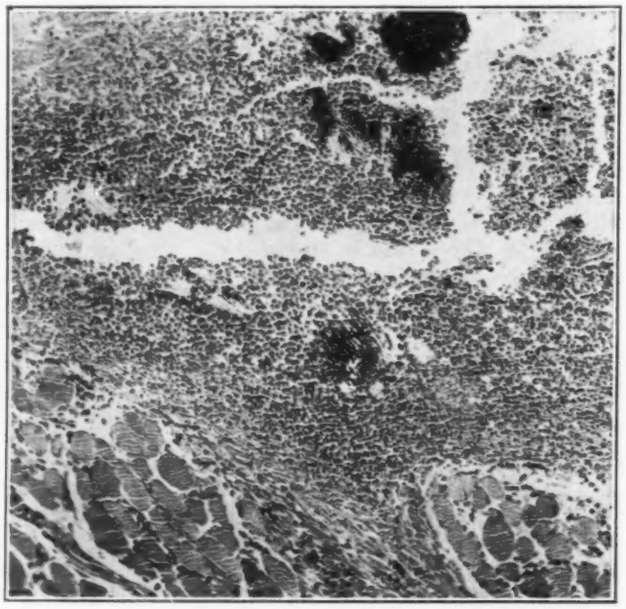

Fig. 3.—After exposure to sulfadiazine, showing frank abscess about remaining clumps of the undissolved drug in the upper and central portion of the illustration. Inflammatory cells are practically all polymorphonuclears with a few large monocytes.

5. Long, L. W., and Dees, J. G.: The Local Use of Sulfanilamide, Surgery **9**: 878 (June) 1941.

Second, after operation for acute appendicitis it is not the local area which is the trouble maker. This can be handled by adequate drainage. The serious complications are distant peritoneal abscess between loops of bowel or subphrenic abscess. These can in no way be altered or prevented by covering the cecum with a sulfonamide powder. The drug is absorbed locally and does reach the distant foci by way of the blood stream but in no greater concentration than if it was given by mouth or parenterally. Therefore it seems useless to expect any added benefit to the patient from a local instillation of the drug. Furthermore, the blood level of sulfonamides given in this manner rises abruptly but is sustained for only a short time. This necessitates parenteral or oral administration to maintain an adequate blood level. At best then the local use of sulfonamides in the peritoneum offers only a lazy means of giving the initial dose of the drug. It by no means sustains a blood level sufficiently high to be effective after the first few hours.

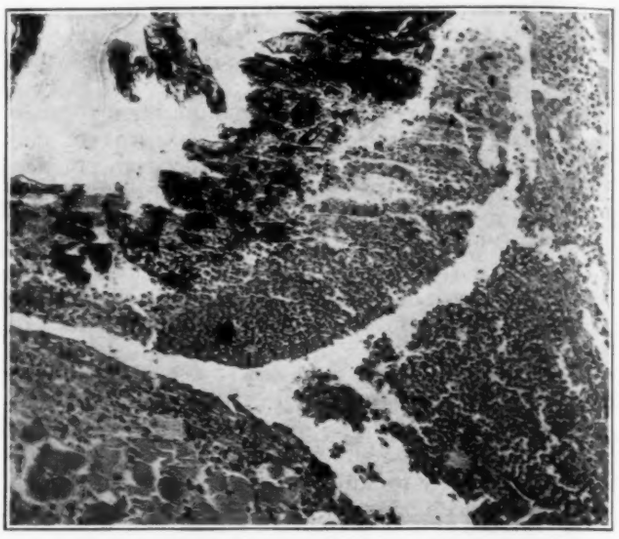

Fig. 4.—Sulfathiazole crystals are shown as dark amorphous masses in upper left. Surrounding them is a mantle of inflammatory cells. There was but little proliferation of fibroblasts in any of the sections at this early three day stage.

Lastly, and probably most important, local sulfonamide implantation gives the operating surgeon a false sense of security. He feels that he has utilized the latest and most modern therapy. The miracles these drugs have performed are well known to the public and the profession alike. The operator feels that there can at least be no harm in their local use. The harm is to the surgeon himself. He places faith in a questionable procedure, a procedure which he possibly has used to replace good careful surgery.

It should be emphasized that the foregoing criticism does not apply to the systemic use of the sulfonamides in cases of severe peritonitis. It is believed that this type of therapy is a permanent addition to surgery and will be more and more frequently used in the future.

SUMMARY

1. All common sulfonamide drugs are irritant to tissues when placed in them in powdered form.

2. The amount of inflammatory reaction which the individual drugs cause is variable. Some are caustic enough to produce actual abscess. All produce an inflammatory reaction.

3. The practice of placing one of these chemical irritants in a clean benign wound is not justified. It seems doubtful that any drug which produces so much damage to tissue cells could possibly be of sufficient value to warrant its use.

4. The implantations of a sulfonamide powder at the site of an appendectomy is also questioned. This practice cannot elevate the concentration of the drug at a distant peritoneal pus pocket above that obtainable by systemic administration.

5. Adhesions may result from application to bare peritoneum.

6. These procedures give the surgeon a false sense of security, to the detriment of sound surgical judgment.

7. This criticism is not in any way directed against the local or systemic use of the sulfonamides in ulcerations or in contaminated wounds which are left open. The same is true of the systemic use of these drugs in cases of severe peritonitis.

614 Hume Mansur Building.

EPIDEMIC OF ENCEPHALITIS, PREDOMINANTLY ST. LOUIS TYPE, IN PINAL COUNTY, ARIZ.

GORDON MEIKLEJOHN, M.D.
AND
WILLIAM McD. HAMMON, M.D., DR. P.H.
SAN FRANCISCO

Encephalomyelitis in horses has been present throughout Arizona for a number of years, but human encephalitis has rarely been reported.[1] During the summer of 1941 equine encephalomyelitis again appeared and soon afterward cases of human encephalitis began to occur in several parts of the state. In Pinal County, in southern Arizona, 18 human cases were studied during the months June to November. All but 3 of the patients were hospitalized. The etiologic diagnosis was established in most instances by repeated virus neutralization tests. Although the coincident equine outbreak pointed toward the western equine strain as the probable cause, the virus neutralization studies suggest that two viruses were responsible, western equine and St. Louis, with the latter greatly predominating. Clinically the cases could not be divided into two groups.

Since the discovery of the St. Louis encephalitis virus during the epidemic of 1933 [2] it has been shown to be widely distributed throughout the United States. By 1937 outbreaks of encephalitis reported as due to the St. Louis virus had occurred in Missouri, Kansas, Illinois, Kentucky, Indiana and Ohio. Virus neutralization tests reported in 1935 [3] suggested that the virus was present in still other areas. In 1934 and succeeding years antibodies to St. Louis virus were found in the bloods of patients in central California who were convalescing from attacks of encephalitis.[4] In 1940 a mixed outbreak of St. Louis and western equine encephalitis was reported from the Yakima Valley in Washington.[5] In 1941 in this area both these viruses were isolated from Culex tarsalis mosquitoes.[6] In addition, it was found that neutralizing antibodies for St. Louis virus were present in serums from many species of domestic and wild mammals and birds [7] and from many normal human beings.[5] Also in 1941 antibodies to this virus were demonstrated in patients from an outbreak in Colorado.[8] Antibodies to the St. Louis virus in the serums of other vertebrates have likewise been reported from California,[9] Colorado,[8] Massachusetts, Texas and Nevada;[10] in the last four states observations were restricted to horses. However, only in the St. Louis area,[2] in Kansas City [11] and in the Yakima Valley [6] has the virus been isolated or the infection proved to be due to this virus by demonstration of an increase in serum antibodies between an early and a late blood specimen.[12] The latter was repeatedly accomplished in the Arizona outbreak, making this the fourth area in the United States where satisfactory criteria for identification have been filled.

EPIDEMIOLOGIC DATA

The area in which this outbreak occurred is a flat triangle of irrigated land, 1,400 feet above sea level, lying south of the Gila River. Most of the land now under cultivation has been reclaimed within the past fifteen years. Cotton is the main crop. The summer heat is intense with maximum daily temperatures averaging 100 F. Rains are few and the humidity is low. Mosquitoes abound, breeding readily in the standing waters which accompany irrigation. Samples collected in the area during this season and sent to Mr. W. C. Reeves of the Department of Entomology of the University of California were identified as Aedes vexans, Anopheles pseudopunctipennis, Culex pipiens, Culex stigmatasoma, Culex tarsalis, Culex quinquefasciatus, Psorophora confinnis and Theobaldia inornata. Of these, Aedes vexans has been shown capable of transmitting the western equine virus in the laboratory, Culex tarsalis has been found infected with both the equine and the St. Louis virus in nature, and Culex pipiens

From the Burton Cairns General Hospital of the Agricultural Workers Health and Medical Association, Casa Grande, Ariz., and the George Williams Hooper Foundation of the University of California (aided by a grant from the National Foundation for Infantile Paralysis, Inc.).

Several physicians in Pinal County permitted us to follow their patients and obtain specimens. The Arizona State Health Department, in particular Mr. G. W. Marx of the Sanitary Engineering Division, cooperated in collecting a large number of the mosquitoes obtained for identification.

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2. Muckenfuss, R. S.; Armstrong, C., and McCordock, H. A.: Encephalitis: Studies on Experimental Transmission, Pub. Health Rep. **48**: 1341-1343 (Nov. 3) 1933. Webster and Fite.[11]

3. Wooley, J. G., and Armstrong, C.: The Distribution of Immunity Against Encephalitis of the St. Louis Type in the United States as Determined by the Serum Protection Test in White Mice, Pub. Health Rep. **49**: 1495-1505 (Dec. 14) 1934. Webster, Fite, Clow and Muench.[12]

4. Wynns, H. L., and Hawley, C. J.: Epidemiology of Epidemic Encephalitis in California, Am. J. Pub. Health **29**: 781-786 (July) 1939. Howitt, B. F.: Viruses of Equine and of St. Louis Encephalitis in Relationship to Human Infections in California 1937-1938, ibid. **29**: 1083-1097 (Oct.) 1939. Buss, W. C., and Howitt, B. F.: Human Equine Encephalomyelitis in Kern County, Calif., 1938, 1939 and 1940, ibid. **31**: 935-944 (Sept.) 1941.

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6. Hammon, W. McD.; Reeves, W. C.; Brookman, B.; Izumi, E. M., and Gjullin, C. M.: Isolation of the Viruses of Western Equine and St. Louis Encephalitis from Culex Tarsalis Mosquitoes, Science **94**: 328-330 (Oct. 3) 1941.

7. Hammon, W. McD.; Gray, J. A., Jr.; Evans, F. C.; Izumi, E. M., and Lundy, H. W.: Western Equine and St. Louis Encephalitis Antibodies in the Sera of Mammals and Birds from an Endemic Area, Science **94**: 305-307 (Sept. 26) 1941. Hammon, W. McD.; Lundy, H. W.; Gray, J. A.; Evans, F. C.; Bang, F., and Izumi, E. M.: A Large Scale Serum Neutralization Survey of Certain Vertebrates as Part of an Epidemiological Study of Encephalitis of the Western Equine and St. Louis Types, to be published.

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10. Hammon, W. McD.; Carle, B. N., and Izumi, E. M.: Infection of Horses with St. Louis Encephalitis Virus, Experimental and Natural, Proc. Soc. Exper. Biol. & Med., to be published.

11. Webster, L. T., and Fite, G. L.: A Virus Encountered in the Study of Material from Cases of Encephalitis in the St. Louis and Kansas City Epidemics of 1933, Science **78**: 463-465 (Nov. 17) 1933.

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has been demonstrated as capable of transmitting the St. Louis virus under laboratory conditions.

The patients studied were all members of the families of migratory agricultural workers; most of them had come to Arizona from Texas or Oklahoma within the preceding three years. These families reside in rural areas on the ranches where they are employed, living under conditions which permit maximal exposure to all environmental factors. Around these ranches are concentrated the relatively few domestic animals and fowl which are raised in the area. The migrant population during the summer season is approximately four thousand. The resident population numbers approximately seven thousand five hundred, of whom three thousand eight hundred reside in three small towns. It is of interest that no cases were reported among the residents of these three towns.

Cases occurred throughout July, August and September, and 1 in November with no epidemic peak. There were 13 cases in males and 5 in females. Seventeen patients were white; the other was a Negro. The age distribution differed from previously reported St. Louis outbreaks in that half the patients were under 12 years of age. The morbidity rate for the migrant population was very high, approximately 450 per hundred thousand, and for the total population of the area approximately 157 per hundred thousand. No deaths occurred, although in all previous outbreaks the case fatality rates have been above 20 per cent. Two additional cases, confirmed by neutralization test, occurred in the adjoining Gila River Indian Reservation, one of which was reported as fatal.

Most of the encephalomyelitis in horses occurred during the latter part of June and July, somewhat before the majority of the human cases, as has been pointed out in numerous instances.[13]

TABLE 1.—*Age, Date of Onset, Clinical and Laboratory Findings, Etiology and Sequelae*

Patient	Age, Years	Date Onset	Peak Temperature, F.	Duration of Fever, Days	Admission Spinal Fluid: Initial Pressure Mm. H_2O	Admission Spinal Fluid: Cell Count, per C.Mm.	Admission Spinal Fluid: M/P Ratio	Admission Spinal Fluid: Pandy	Admission Spinal Fluid: White Blood Count, per C.Mm.	Apparent Cause *	Present Status
H. B.	8/12	11/ 2	103.2	8	.....	80	8/2	.....	13,000	St. L.	normal
P. B.	1 2/12	8/25	103.1	9	.....	220	7/3	+	20,500	St. L. & W. E.	slight mental change
C. C.	1 5/12	8/28	104.6	8	.....	140	9/1	++	15,200	uncertain	slight mental change
E. W.	3	9/18	105.4	8	.....	50	4/6	++	27,200	uncertain	slight mental change
P. M.	4	7/18	103.2	6	.....	70	8/2	±	32,000	uncertain	normal
B. L. S.	4	7/19	102.0	8	.....	70	7/3	0	.....	uncertain	normal
M. H.	4	9/11	103.6	8	.....	120	6/4	+	15,500	St. L.	normal
C. A.	11	9/25	101.0	8	170	160	6/4	+	14,600	St. L.	normal
W. M.	16	7/22	104.1	11	215	205	6/4	±	10,000	St. L. & W. E.	severe c.n.s. damage
L. K.	18	8/25	101.0	7	205	65	8/2	+	10,300	St. L.	normal
M. M.	24	8/21	105.2	11	235	230	6/4	+	13,000	St. L.	slight mental change
B. S.	25	6/27	105.2	11	.....	45	10/0	+	15,500	St. L. & W. E.	moderate mental change
B. B.	48	8/15	104.0	7	175	45	8/2	0	14,500	St. L.	normal
O. H.	60	7/23	101.3	6	270	75	8/2	±	8,800	uncertain	normal
W. W.	62	9/19	104.2	9	145	80	4/6	+	11,900	St. L.	normal
J. H.	64	9/ 5	103.0	9	205	40	9/1	+	13,300	St. L.	normal

* See table 2.

CLINICAL FEATURES

The clinical and laboratory findings show no significant variation from those described in connection with the large St. Louis outbreaks.[14] Some of the salient features of these data for each case are listed in table 1.

There was no clearcut prodrome. Frequently persons who were working in the fields on one day were seriously ill on the next. In adults the illness began with malaise, headache and aches in the back and the abdomen. The headache was at first occipital, later frontal as well, and was characteristically described as the worst the patient had ever had. Photophobia was present in varying degrees. Drowsiness was usually present. Temperature rose to a peak ranging from 101 to 106 F. within three days and fell gradually over a variable period which paralleled the severity of the illness. The average duration of fever was eight days. Nausea and vomiting were infrequently noted, a contrast to Hammon's findings in Yakima.[15] In children the picture was far less distinctive. Irritability and drowsiness were common and convulsions were rare, in contrast to the described outbreaks of western and eastern equine encephalitis in small children. The diagnosis was usually suggested by the sustained fever.

The mental state varied from a slight drowsiness to deep coma. Neck stiffness and a positive Kernig sign were uniformly present, but only in exceptional instances did neck rigidity resemble that found in purulent meningitis. Abnormal neurologic findings were noted only in the more severe cases. These included tremor, ataxia, spasticity, nystagmus and altered deep reflexes. Puffiness of the face was in certain instances very noticeable. Persistent hiccup was noted in 1 case. Thrombophlebitis of the leg complicated the convalescence of 1.

Eight of the 18 cases were of sufficient severity to cause doubt concerning the patient's survival. Two of these patients were under 5 years of age, 4 between 5 and 50 and 2 over 60. Significant laboratory data are summarized in table 1.

CASE SUMMARY

The following report illustrates the features of a severe case:

W. M., a youth aged 16 years, came to Arizona from Oklahoma in late June 1941. During the following month he slept in the back seat of an automobile in an area infested with mosquitoes. On July 22 he became ill quite suddenly, complaining of headache, malaise, abdominal pain and pains in his arms and legs. He became increasingly drowsy. On July 26 he was admitted to the hospital. At this time he gave a coherent story of his illness. Physical examination showed neck stiffness, a positive Kernig sign, nystagmus and mental dulness. The temperature was 103.6 F. The white blood cell count was 12,500 with a differential count showing polymorphonuclears 68 per

13. Hammon and Howitt.[5] Hammon, Lundy, Gray, Evans, Bang and Izumi.[7]

14. Bozalis, G. S., and Jones, A. B.: Epidemic Encephalitis, St. Louis Type: Survey of Outbreak, Summer and Fall of 1937, J. Oklahoma M. A. **31:** 164-171 (May) 1938. Pub. Health Bull. 214, Report of the St. Louis Outbreak of Encephalitis, June 1935.

15. Hammon, W. Mc.D.: Encephalitis in the Yakima Valley: Mixed St. Louis and Western Equine Types, J. A. M. A. **117:** 161-167 (July) 1941.

cent, lymphocytes 25 per cent and monocytes 7 per cent. Lumbar puncture showed an initial pressure of 215 mm. of water, normal excursion with jugular compression, cell count 205, mononuclear/polymorphonuclear ratio 6/4, Pandy positive. On July 29 the temperature was 103.2 F. The patient was completely irrational, incontinent, aphasic and grimacing. Thereafter the mental state remained much the same. On August 2 tremor and ataxia were severe. On August 16 he was discharged. The facial expression was fixed and he was still unable to talk or walk without help. Communications received two months later stated that he had improved considerably but showed extensive nervous system damage. Neutralization tests were made on three blood specimens. On the sixth day of illness they were negative. On the twenty-seventh and seventy-eighth days of illness they were 2 plus for the western equine and 1 plus for the St. Louis type.

NEUTRALIZATION TESTS

As will be noted in table 2, in which the results of all neutralization tests are presented, for most cases two blood specimens were tested and for many three. All were tested under carefully controlled conditions by the intracerebral mouse test described by Hammon and Izumi.[16] All serums were tested when fresh, for it has been noted by others[17] as well as by one of us (W. McD. H.) that antibodies to the St. Louis virus decrease during storage. As has been pointed out in other studies,[18] it will be noted that antibody response to the St. Louis virus is relatively slow.

TABLE 2.—*Results of Neutralization Tests*

Patient	Days After Onset When Bled: Early	Inter-mediate	Late	Results of Tests: St. Louis: Early	Inter-mediate	Late	Western Equine: Early	Inter-mediate	Late	Apparent Cause
M. M.	6	21	66	0	0	++	0	0	0	
B. B.	6	25	80	0	±	++	0	0	0	
M. H.	6	....	59	0	—	++	0	.....	0	
W. W.	4	12	51	±	++	++	0	0	0	
J. H.	6	....	92	±	.....	++	0	.....	0	St. Louis
L. K.	9	....	84	+	.....	++	0	—	0	
H. B.	5	....	35	0	.....	+	0	.....	0	
C. A.	6	....	41	0	.....	++	0	.....	±	
W. M.	6	27	78	0	+	+	0	++	++	St. Louis
P. B.	5	....	69	0	.....	++	+	.....	++	and western
B. S.	..	25	59	....	0	+	....	±	++	equine
T. E.	..	....	100	....	.....	++	....	.....	0	Uncertain
C. C.	..	....	32	....	—	+	....	—	0	(no early
B. L. S.	..	14	.....	—	+	.....	....	0	.....	speci-
G. E.	..	....	105	....	.....	+	....	.....	++	men)
E. W.	5	11	76	+	+	—	0	0	0	Uncertain
O. H.	5	20	.....	+	±	.....	+	+	.....	(no change
P. M.	6	....	114	0	.....	0	+	.....	+	in titer)

The cases are grouped in table 2 according to the results of the neutralization tests. In the first group are 8 that showed a definite rise in titer to the St. Louis virus but developed no antibodies to the equine virus. The next group, 3 in number, is composed of those who showed a rise in titer to both viruses. In the third group are those in which only late specimens were obtained, all 4 with antibodies to the St. Louis virus and 1 to the equine in addition. No definite conclusions can be drawn in respect to these, although, since antibody to the equine virus is seldom encountered without history of a clinical infection, the evidence for equine infection in the 1 with equine antibodies (G. E.) can be considered presumptive. The other 3 patients were all very young children, so their St. Louis antibodies are possibly significant. In the last group are 3 who show no rise in titer from an early to a late specimen. Low titers to one virus or both occurred in all. These also cannot be classified. However, several observations may be made which suggest a possible interpretation. A glance at table 1 shows that 4 of the "uncertain" group fall in the low age bracket ($1\frac{5}{12}$ to 4 years). Also it will be noted that 4 of the 6 patients 4 years of age or less showed no titer at any time for either virus above 1 plus. This poor antibody response may be characteristic of the lower age group.

One is naturally hesitant to assume that two etiologic agents are involved in one epidemic and especially that simultaneous double infection occurs in the same individual, although parallel examples now exist of similar immunologic findings in the group of influenzas. However, such definite evidence of antibody formation to both viruses as we have in patients W. M., P. B. and B. S., even if it was an isolated instance, would constitute evidence of a strongly suggestive nature. As has been pointed out, in Yakima,[5] where findings of a somewhat similar nature were encountered, definite proof of the presence and close association of the two viruses was eventually obtained by repeatedly finding them in the same species of mosquito. Here the immunologic evidence for St. Louis virus infection is indisputable in 11 cases. In addition to the immunologic evidence for the equine infection, the recognition of equine encephalomyelitis in this area greatly strengthens the evidence of the presence and activity of this second virus.

Although the number of observations is small, it may be of some significance that the 2 patients with the most severe residual central nervous system damage (W. M. and B. S., table 1) developed antibody to both viruses during the course of the illness, and the 1 other patient (P. B.) for whom we have similar evidence of double infection also suffers from residual damage.

At least one serum from almost every patient was tested against the eastern equine virus, but no positives were found.

DIAGNOSIS

The diagnosis is suggested by sustained fever, severe headache and signs of meningeal irritation and an elevated spinal fluid white cell count. However, in order to establish an etiologic diagnosis it is necessary

16. Hammon, W. Mc.D., and Izumi, E. M.: A Virus Neutralization Test Subject to Standardization: Used with Western Equine Encephalomyelitis, St. Louis Encephalitis and Mouse Adapted Poliomyelitis Viruses, J. Immunol. **43**: 149-157 (Feb.) 1942.

17. Webster, L. T.; Fite, G. L.; Clow, A. D., and Muench, H.: Experimental Studies on Encephalitis: Specific Inactivation of Virus by Sera from Persons Exposed to Encephalitis, St. Louis Type 1933, J. Exper. Med. **62**: 827-847 (Dec.) 1935.

18. Webster and Fite.[11] Hammon.[15] Hammon and Howitt.[5] Smith and Moore.[12]

either to isolate the virus or to demonstrate a rise in serum antibodies during the course of the illness. Single late blood studies tend to mislead, for in many areas of the United States persons may acquire antibody to encephalitic viruses without ever having developed a clinically recognizable encephalitis.

SEQUELAE

Twelve of the 18 patients showed no apparent residue. Six showed definite mental impairment at the time of discharge from the hospital. All but 1 of these improved greatly during the ensuing six weeks, though they did not recover completely. Of the latter 2 were adults and 3 were children. One patient showed severe, undoubtedly permanent, mental and motor damage. His case, W. M., has been described in detail.

TREATMENT

The small number of cases makes it impossible to draw any conclusions about the efficiency of treatment. Two patients who had received no sulfonamide therapy turned out very badly. Thereafter all patients seen early received full doses of one of the sulfonamide drugs, mostly sulfadiazine. The effect of this drug was in no case dramatic, and it is questionable whether it had any effect at all. As yet there is no support for the effectiveness of the sulfonamides against the encephalitic viruses in experimental animals, and there is some negative evidence. However, in view of the fact that no deaths occurred in this series, judgment on the efficacy of this drug should be reserved. On the basis of the greater than 20 per cent case fatality in other St. Louis type epidemics, at least four or five deaths would be expected in this group.

SUMMARY

An epidemic of encephalitis occurred in Pinal County, Ariz., among migratory laborers. There were 18 cases, 15 of which were hospitalized. At least one serum from all was tested against both the St. Louis and the western equine viruses. The blood of all but 1 neutralized the St. Louis virus at some time. Eleven of 14 patients whose blood was tested more than once were shown to have developed antibody to this virus during the course of the illness, and 3 of these also developed antibody to the equine virus during the same interval. Half the patients were children under 12 years of age. No deaths occurred, but 6 have at present some residual central nervous system damage, one of a severe degree.

Intestinal Bacteria.—In the average adult it is estimated that each day's food in its passage through the digestive tract is subjected to the action of over one hundred billion bacteria, chiefly in the large intestine. . . . If it were possible to exclude absolutely all bacteria from the digestive tract, the well-being of the body would probably not be impaired; yet under such conditions as ordinarily exist, the bacteria which usually predominate in the digestive tract of the thoroughly healthy man probably render an important service in helping to protect against noxious species. Lactobacillus acidophilus has come to be regarded as the species best adapted to the function of maintaining a favorable condition in the human intestine. The taking of cultures of this organism and the liberal consumption of lactose and dextrin, the carbohydrates most favorable to it, may assist in the establishment and maintenance of a good condition of intestinal hygiene.—Sherman, Henry C.: Chemistry of Food and Nutrition, New York, Macmillan Company, 1941.

THE TYPHOID CARRIER PROBLEM

REPORT OF A STUDY OF ONE HUNDRED AND TEN TYPHOID CARRIERS AT THE MANTENO STATE HOSPITAL, MANTENO, ILL.

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The medical and economic importance of the typhoid carrier problem is readily estimated when one realizes that as many as 44 per cent of all cases of typhoid are due to carriers.[1] Gay[2] in 1918 stated that 150,000 cases of typhoid occur yearly in the United States with an annual production of approximately 7,500 carriers. Cumming[3] calculated that in Washington, D. C., in 1930, twenty years after commencement of preventive measures against typhoid, there were 671 carriers per hundred thousand of the population. Stebbins[4] estimated that as of Jan. 1, 1936 there were approximately 5,000 typhoid carriers in New York State exclusive of New York City. This city reported 405 chronic typhoid carriers under the supervision of the department of health as of July 1, 1936.[5] At the close of 1939 there were 422 typhoid carriers under supervision in upstate New York.[6] Bigelow and Anderson[7] estimated 1,100 typhoid carriers in the state of Massachusetts in 1933.

The part played by human carriers in the spread of typhoid fever was first clearly recognized by Robert Koch[8] in his famous address of November 1902. Even at that time he considered the typhoid patient or convalescent as the most fruitful source of further infection.

Today, almost forty years later, it is interesting to note that at a recent symposium on the typhoid carrier problem held at the New York Post Graduate Hospital[9] it was agreed that during the past five years no cases of typhoid due to contaminated water supply had occurred in the state of New York, while carriers have been directly responsible for a large proportion of cases. Knowlton[10] reports that in the state of Connecticut not a single case of typhoid was traced to water, food or milk during the past four years.

The first authentic typhoid carrier in this country, Typhoid Mary of New York, was reported in THE

From the Manteno State Hospital.
The sulfaguanidine used in this study was supplied by E. R. Squibb & Sons.
Dr. H. J. Shaughnessy of the State Public Health Laboratory conducted the bacteriologic work in this study; Dr. M. S. Palmer of the Manteno State Hospital did the x-ray work and Dr. D. J. Cohn of Michael Reese Hospital made the blood determinations of sulfaguanidine.

1. Garbat, A. L.: Typhoid Carriers and Typhoid Immunity, Monograph 16, New York, Rockefeller Institute for Medical Research, May 1922.
2. Gay, F. P.: Typhoid Fever, New York, Macmillan Company, 1918.
3. Cumming, J. G.: Should Barriers Against Typhoid Be Continued? J. A. M. A. **98:** 93 (Jan. 9) 1932.
4. Stebbins, E. L.: The Detection and Control of Typhoid Carriers, symposium on the typhoid carrier problem at the New York Post Graduate Hospital, June 6, 1936.
5. Frant, S.: The Typhoid Carrier Situation in New York City, symposium on the typhoid carrier problem at the New York Post Graduate Hospital, June 6, 1936.
6. Report on Typhoid Carriers, New York News, J. A. M. A. **115:** 790 (Aug. 31) 1940.
7. Bigelow, G. H., and Anderson, G. W.: Cure of Typhoid Carriers, J. A. M. A. **101:** 348 (July 29) 1933.
8. Koch, Robert: Sitzung des wissenschaftlichen Senates bei der Kaiser Wilhelms Akademie, Nov. 28, 1902.
9. Hanssen, E. C.: The Present Status of the Typhoid Carrier Problem, New York State J. Med. **39:** 1347 (July 15) 1939.
10. Knowlton, M.: The Typhoid Carrier Problem in Connecticut, symposium on the typhoid carrier problem at the New York Post Graduate Hospital, June 6, 1936.

JOURNAL in 1907.[11] Her life history has been the subject of a recent biography.[12] To her 51 cases of typhoid and three deaths were attributed.

Ever since, the management of typhoid carriers has presented a most difficult problem to the various health agencies. Numerous states have special regulations for dealing with typhoid carriers. For example, the regulations of the Department of Health of New York City for the supervision of typhoid carriers (1922) forbid them to handle food or drink intended for the use of others or to send clothing to the laundry before disinfection. The movements and whereabouts of carriers must be reported to the department and their discharges examined from time to time. Rules are laid down regarding personal hygiene and the disposal of excreta.[13] In the state of Illinois carriers are prevented from engaging in certain occupations such as food handling and dairy work and are supervised in order to avoid the spread of the disease.[14]

As compared with the carrier who is sane, the control of the typhoid carrier in hospitals caring for mentally ill patients is even more difficult. Such persons are a continual menace both to inmates and attendants and often are the cause of repeated outbreaks of the infection. In Scotland all known psychotic carriers are segregated in a single institution.[15]

The present study is the outcome of clinical, bacteriologic and therapeutic observations conducted on

TABLE 1.—*Number and Percentage of Carriers With or Without Previous Active Typhoid Disease*

Total number of carriers	110	
Number of carriers with previous active disease	54	49.1%
Number of carriers without previous active disease	56	50.9%

110 typhoid carriers at the Manteno State Hospital extending over a period of one year. A violent outbreak of typhoid in 1939 was followed by a typhoid carrier state in numerous patients who did or did not have signs of active disease during the epidemic (table 1). These patients were segregated in a single unit so that hygienic as well as medical procedures could be carried out with a minimum of danger to the environment and with a maximum of efficiency.

CLINICAL OBSERVATIONS

In general, all patients felt remarkably well, and there was no evidence by way of physical examination to indicate the typhoid carrier state. There was nothing to demonstrate a lowered resistance or an increased susceptibility toward infection. In view of the well known involvement of the biliary tract and gallbladder in typhoid, particular attention was paid to clinical or roentgen evidence of gallbladder disease. There were 7 female carriers who experienced more or less severe attacks of pain in the right upper part of the abdomen associated with vomiting, nausea and a subicteric state. The attacks were interpreted as biliary colics. Cholecystograms performed on 80 carriers revealed gallbladder disease in 57 cases as evidenced by lack of dye concentration, nonfilling of the gallbladder and the presence of calculi in 6 cases (table 2).

11. Soper, G. A.: The Work of a Chronic Typhoid Germ Distributor, J. A. M. A. **48**: 2019 (June 15) 1907.
12. Soper, G. A.: The Curious Career of Typhoid Mary, Bull. New York Acad. Med. **15**: 698 (Oct.) 1939.
13. Browning, C. H.: Chronic Enteric Carriers and Their Treatment, Medical Research Council, Special Report Series, No. 179, London, His Majesty's Stationery Office, 1933.
14. Statement of Department of Public Health, State of Illinois, Chicago M. Soc. Bull. **42**: 8 (July 1) 1939.
15. Fifteenth Annual Report of the General Board of Control, Edinburgh, 1929 (cited by Browning [13]).

AGE AND SEX

Table 3 shows a striking preponderance of females in our series.

Uhlenhuth [16] states that 80 per cent of typhoid carriers are adult females. Children have rarely been reported as being typhoid carriers. The frequency of disorders of the biliary tract in older women seems to be responsible

TABLE 2.—*Number and Percentage of Eighty Carriers With and Without Roentgen Evidence of Gallbladder Disease*

Total number of carriers examined	80	
Number of carriers with x-ray evidence of gallbladder disease	57	71.3%
Number of carriers without x-ray evidence of gallbladder disease	23	28.8%

TABLE 3.—*Distribution of Sex Among One Hundred and Ten Typhoid Carriers*

Sex	Number	Per Cent
Females	76	69.1
Males	34	30.9

for the preponderance of females among typhoid carriers. The opinion has been expressed that a typhoid carrier does not have as great a life expectancy as a person of the same age in the general population.[17] Our series does not substantiate this point of view. Classification according to age (table 4) revealed most of the patients in the age group between 40 and 60. There were 45 patients past the age of 50, 15 past the age of 60 and 4 past the age of 70. The oldest typhoid carrier on record seems to be the 1 reported recently in THE JOURNAL,[18] a woman aged 101 who has probably been a typhoid carrier for eighty years. The importance of age will be referred to in our discussion concerning surgical therapeutic procedures.

TABLE 4.—*Respective Age Group Among One Hundred and Ten Typhoid Carriers*

Age Group	Number	Per Cent
20-30	11	10
30-40	23	20.9
40-50	31	28.2
50-60	30	27.3
60-70	11	10
70-80	3	2.7
80-90	1	0.9

TABLE 5.—*Bacteriologic Classification of One Hundred and Ten Typhoid Carriers*

	Number	Per Cent
Bile carriers	65	59.1
Intestinal carriers	43	39.1
Urinary carriers	2	1.8

CLASSIFICATION OF CASES

The cases were classified into bile, intestinal and urinary carriers (table 5). The bile carrier state was determined by bacteriologic examination of bile obtained through duodenal drainage. A Rehfuss tube was introduced in the morning on a fasting stomach and was allowed to remain until duodenal fluid was obtained.

16. Uhlenhuth, P.: Das Problem der Typhusbazillenträger und ihre Bekämpfung, Med. Klin. **30**: 789 (June 15) 1934.
17. Forsbeck, F. C.: Blood Pressure of Typhoid Carriers, Science **80**: 478 (Nov. 23) 1934.
18. A Typhoid Carrier at 101, New York News, J. A. M. A. **114**: 1276 (March 30) 1940.

Forty cc. of olive oil was then injected into the duodenum, which usually was followed by production of dark gallbladder bile within fifteen minutes. Olive oil was considered preferable to magnesium sulfate because of the possible germicide action of the latter.

In contradistinction to previous reports,[19] we have found in our series that as many as eight intubations were necessary in order to determine the presence or absence of the bile carrier state (table 6). Fecal carriers whose bile was negative after eight intubations were classified as intestinal carriers. There were only 2 urinary carriers in our series, both of whom were also fecal carriers.

TABLE 6.—*The Necessity of Repeated Duodenal Drainage in Order to Determine Definitely the Bile Carrier State*

	Number of Carriers in Whom Positive Bile Cultures Were Obtained	Per Cent
First duodenal drainage	27	41.5
Second duodenal drainage	11	16.9
Third duodenal drainage	6	9.2
Fourth duodenal drainage	10	15.4
Fifth duodenal drainage	7	10.8
Sixth duodenal drainage	3	4.6
Seventh duodenal drainage	1	1.5

All in all, out of 110 fecal carriers, 15 could not be submitted to biliary drainage owing to lack of cooperation. Out of 95 persons submitted to biliary drainage 65, or 68.4 per cent, were found to be bile carriers. An attempt to further subdivide bile carriers into liver and gallbladder carriers proved unsuccessful in our hands. Aside from difficulties in differentiating between "liver bile and gallbladder bile," the samples, when obtained, were uniformly either positive or negative.

THERAPEUTIC OBSERVATIONS WITH SOLUBLE IODOPHTHALEIN

In a previous communication by Saphir and Howell,[20] experiments were reported as to the in vitro action of soluble iodophthalein on the bacteria of the typhoid-paratyphoid group. It was found that the dye in dilution of 1:30 retarded the growth of typhoid bacilli in one hour, while two hour contact resulted in death of typhoid bacilli. Previously, Onodera and his associates[21] had reported a strongly germicidal action of the dye on typhoid bacilli, whereas Nickel[22] found that soluble iodophthalein had a decided bacteriostatic action in vitro on staphylococci and streptococci, destroying them in dilution of 1:20 in ten minutes. However, he observed only slight action on gram-negative bacilli of the colityphoid group. In his studies he found that intravenous injection of soluble iodophthalein prevented streptococcic invasion of the gallbladder of rabbits.

Clinically, 1 paratyphoid carrier reported by Saphir and Howell[20] and 1 typhoid carrier reported by Enright[23] were apparently cured by treatment with soluble iodophthalein.

It was therefore considered justified to try this form of treatment on a larger series of cases under controlled conditions. A priori it was expected that only bile positive cases would benefit from treatment with a biliary antiseptic, and it was therefore decided to submit our 65 bile carriers to treatment.

Four Gm. of soluble iodophthalein was administered orally in orange juice three times a week until a total of forty doses had been given. The patients were kept on a low fat diet in order to avoid, if possible, unnecessary contractions of the gallbladder. For the same reason the dye was given in the early morning so that the maximum dye concentration in the gallbladder was reached at night when rest and absence of food intake might permit the gallbladder to remain quiescent. Thus optimum conditions for a full bactericide effect on bacilli in the gallbladder could be anticipated.

No ill effect was observed from the treatment except some nausea and occasional vomiting following the administration of the dye. In a few cases a mild to moderate diarrhea developed, apparently due to the phenolphthalein content of the drug. This, however, could be easily controlled by ordinary antidiarrheic measures and in no case required cessation of treatment.

RESULTS

Out of 65 bile carriers treated, in 21, or in 32.3 per cent, sterilization of bile was obtained (table 7). Criteria for sterilization of bile were three negative bacteriologic reports of bile, obtained through duodenal drainage on three subsequent occasions.

To our great disappointment we found that 16 out of the 21 persons whose bile became sterile continued to excrete typhoid bacilli in the stools. It thus became apparent that in spite of the apparently cured bile carrier state, an additional intestinal carrier state was present in these 16 instances. It is quite conceivable that the typhoid infected bile in passing through the intestinal tract for a prolonged period of time may set up additional "typhoid foci" in the intestinal tract from which bacilli continue to be excreted, an opinion expressed by Garbat.[1] Consequently, only 5, or 7.6 per cent, of the treated persons were considered cured from the typhoid carrier state up to the present writing. The criterion for cure was the absence of typhoid bacilli from at least 10 consecutive stool specimens over a period of at least four months.

Unfortunately, there is no way of determining an additional intestinal carrier state in a bile carrier. It is only after sterilization of bile that the true nature of the carrier state becomes apparent, because of the continuation of excretion of typhoid bacilli in the feces. This excretion may be intermittent and difficult to detect. Some of our treated patients had as many as ten weekly consecutive negative stool reports before a positive culture was obtained. It is for this reason that the criteria for cure were adopted.

TABLE 7.—*Results of Treatment with Soluble Iodophthalein of Sixty-Five Bile Carriers*

Total number treated	65
Number in whom sterilization of bile was obtained	21 or 32.3%
Number in whom sterilization of stool was obtained	5 or 7.6%

Why was sterilization of bile obtained in only 32 per cent of the persons treated?

As already stated, only a concentration of 1:30 acting for two hours will permit soluble iodophthalein to destroy typhoid bacilli. Apparently the anatomic con-

19. Forsbeck, F. C., and Hollon, H. C.: Standards for Determining the Suitability of Bile Specimens for Detection or Release of Typhoid Carriers, Am. J. Pub. Health **27**: 253 (March) 1937.

20. Saphir, William, and Howell, Katherine M.: Soluble Iodophthalein in Treatment of Carriers of Typhoid-Paratyphoid Group, J. A. M. A. **114**: 1988 (May 18) 1940.

21. Onodera, N.; Murakawa, G., and Liu, S.: Ueber eine neue Behandlung von Typhusbazillentraegern, Deutsch. Arch. f. klin. Med. **171**: 503, 1931.

22. Nickel, A. C.: Tetiothalein Sodium-N. N. R. (Tetraiodophenolphthalein) as an Antiseptic and a Germicide of the Biliary Tract, J. Pharmacol. & Exper. Therap. **37**: 359 (Nov.) 1929.

23. Enright, J. R.: Apparent Cure of a Typhoid Carrier with Soluble Iodophthalein, J. A. M. A. **116**: 220 (Jan. 18) 1941.

ditions of the biliary tract and the gallbladder were unfavorable to such concentrated and prolonged action on typhoid bacilli in those cases which did not respond. This does not seem surprising in view of the frequency of biliary tract disease in typhoid infections. Lack of concentration power of the gallbladder as determined by cholecystograms was frequently present in our series. All our cured patients showed a normal response to cholecystography.

THERAPEUTIC ATTEMPTS WITH SULFAGUANIDINE

Marshall and others [24] have reported curative results with sulfaguanidine in the treatment of acute bacillary dysentery. In preference to other sulfonamide compounds, sulfaguanidine is considered to be of particular value in the treatment of enteric infections because of its slow absorption from the intestinal tract, thus exerting a prolonged effect on enteric bacteria. In a recent paper Levi and Willen [25] reported curative results with sulfaguanidine in a typhoid carrier.

We were especially interested in treating those carriers with sulfaguanidine whose bile was free from typhoid bacilli, either as the result of treatment with soluble iodophthalein or because of the finding of bacilli in the feces in the presence of negative bile throughout the study.

Five such patients were treated with sulfaguanidine. The dose given was 0.05 Gm. per kilogram of body weight four times daily for a total period of two weeks. There were no severe reactions from the administration of the drug, although some vomiting, slight elevation of temperature, conjunctivitis and cystitis were observed. However, the symptoms were comparatively mild and cessation of treatment was not required. Sulfaguanidine blood levels were determined and were found not to exceed 1.2 mg. per hundred cubic centimeters.

The results were uniformly unsatisfactory. In all cases in which treatment was given the bacillary excretion continued unabated.

COMMENT

Once the typhoid carrier is detected, the problem resolves itself into the question of whether the carrier should be treated or just controlled. If controlled carriers were not a source of danger to the community, we could not contend that they must be treated.[9] However, the literature mentioned provided ample proof of the danger of spreading typhoid through carriers in spite of measures taken to control their activities.

In view of the absence of legislative measures compelling treatment, we believe that treatment should be urged as a measure intended primarily to benefit the carrier rather than to protect the community.

In spite of many attempts to evolve a cure for the typhoid carrier state, the most extensive review of this subject in recent years [13] reveals that "drug treatment, chemotherapy, measures aimed at alteration of the reaction of the flora of the intestines and vaccine therapy have all proved ineffective."

In 1936 the Royal Medico-Psychological Association of England appointed a committee to study the treatment of enteric carriers in psychopathic hospitals.[26] After considering all the evidence, the committee recommended that cholecystectomy appears to be the only treatment which has any reasonable chance of success, unless the patient is a urinary carrier, in which case cholecystectomy is useless.

The value of cholecystectomy in the treatment of typhoid carriers is well established. This is particularly true when, through the use of duodenal drainage, the bile is found to contain typhoid bacilli.[7]

In the light of our study it would seem that treatment with soluble iodophthalein should be given serious consideration before cholecystectomy is resorted to. The indications for the two forms of treatment are the same, namely the presence of typhoid bacilli in the bile. The results will be problematic if typhoid bacilli are not found in the bile. However, we have presented the difficulties in definitely ruling out the bile carrier state. In our series, eight consecutive biliary drainages were necessary before the presence or absence of the biliary carrier state could be ascertained. It therefore may be worthy of trial to treat a questionable fecal carrier with soluble iodophthalein.

Cholecystectomy has effected cure in 75 per cent of the cases according to some statistics.[13] Our results with soluble iodophthalein have been less striking. Sterilization of bile was obtained in 32.3 per cent and complete cure in only 7.6 per cent of the persons treated.

We wish, however, to emphasize the following factors in favor of our conservative treatment. First, the safety of the treatment in our hands as compared with the mortality of cholecystectomy, particularly in the age group over 50. In our series there were 45 persons, or 40.9 per cent, past the age of 50. Second, the treatment as outlined was our first and necessarily experimental attempt toward a cure. It may well be that changes in dosage, duration of treatment and time interval may improve the results. Finally, all our treated patients were known carriers for more than two years. It is well known that the longer the typhoid carrier state persists, the more difficult the eradication of typhoid bacilli is apt to be. The old dictum "once a typhoid carrier, always a chronic typhoid carrier" gives ample testimony to the futility of therapeutic attempts in the past. Had we not permitted the carrier state to persist too long and thus to set up additional intestinal typhoid foci which cannot be eradicated either by cholecystectomy or soluble iodophthalein, it is our belief that the percentage of cures might have been higher.

SUMMARY AND CONCLUSIONS

1. Clinical, bacteriologic and therapeutic studies on 110 typhoid carriers bring out the difficulties inherent to the typhoid carrier's problem.

2. Treatment with sulfaguanidine in 5 cases had no effect on the bacillary excretion in the stool.

3. The oral treatment with soluble iodophthalein of 65 bile carriers sterilized the bile in 32.3 per cent and freed the stool from typhoid bacilli in 7.6 per cent of the carriers.

4. Treatment with soluble iodophthalein should be given consideration before cholecystectomy is resorted to, particularly in bile carriers past 50 and in the presence of a well functioning gallbladder, as determined by the cholecystogram.

104 South Michigan Avenue.

24. Marshall, E. K., Jr.; Bratton, A. C.; Edwards, L. B., and Walker, E.: Sulfanylguanidine in the Treatment of Acute Bacillary Dysenteria in Children, Bull. Johns Hopkins Hosp. **68:** 94 (Jan.) 1941.

25. Levi, J. E., and Willen, Abner: The Typhoid Carrier State Treated with Sulfaguanidine, J. A. M. A. **116:** 2258 (May 17) 1941.

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IS LYMPHOSARCOMA CURABLE?

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In 1926 Minot and Isaacs [1] published a paper on lymphoblastoma. By that term they meant to include leukemia, Hodgkin's disease, lymphosarcoma and allied disorders. After a careful statistical study of 477 cases they came to the conclusion that all these diseases were incurable. They found that about 10 per cent of the patients had had the disease for six years or longer. Although a number of patients who survived for a long time had been treated by roentgen rays, surgery or a combination of the two, there were some who had received no curative treatment, and the authors felt that it was not possible to conclude that any had been cured by treatment even though they could not deny definite amelioration in some cases.

Since that time there have been remarkably few studies of the results of treatment of this group as a whole, and of lymphosarcoma in particular. Most of the studies made have tended to confirm the opinions expressed by Minot and Isaacs. Desjardins [2] in 1932 stated that "permanent cure of lymphosarcoma is unknown." He felt that radiotherapy might prolong life but was opposed to surgery. Krumbhaar [3] in 1936 remarked that "the lymphomatoid diseases are practically all alike in having a fatal prognosis, though the duration may extend from a few days to many years."

The most important recent study of lymphosarcoma in general is by Sugarbaker and Craver [4] from the Memorial Hospital, New York. This includes a group of 196 patients seen during the twenty year period ending in 1938. For purposes of survival studies they excluded recent patients and those who died or were lost without recurrence. This left 132 patients. Twenty-one of these (15.9 per cent) survived five years. Seven of them either died of lymphosarcoma or had the disease persisting when last seen, leaving only 14, or 10.6 per cent, free from disease after treatment.

Sugarbaker and Craver list five factors which influence the course of the disease: 1. Individual inherent qualities for growth and dissemination in the different tumors, i. e., many run a rapid course but a few may be very slow. Microscopic examination they find does not help one in foretelling this, although in general the giant follicle lymphosarcomas run a less rapid course. 2. The extent of the disease on admission. Only 4 of 21 patients who survived long had clinical evidence of disease in more than two contiguous areas. 3. The location of the primary lesion. The results were better when the primary site was in the head end of the body (23 per cent five year survivals and 15.4 per cent symptom free).[5] Sugarbaker and Craver had no patients who survived long when the primary lesion was in the gastrointestinal tract, which is contrary to the experience of others. 4. Complicating leukemia and pseudoleukemia. Of their series 6.6 per cent of the patients had leukemia and all died. 5. Age. The average survival rate of the 0-29 year age group was only eleven and three-tenths months, while for later age groups it was more than twice that figure. As will be seen, the present study confirms these observations except with regard to histology and the gastrointestinal tract.

TABLE 1.—*Lymphosarcoma (1915-1935 Inclusive)*

Primary Site	Number of Cases	Survived 5+ Years		Died or Alive Symptom with Tumor After 5 Years		Symptom Free 5+ Years, per Cent
		No.	Per Cent	No.	Per Cent	
A—All Cases						
Cervical nodes	45	7	15.6	1	2.2	13.4
Axillary nodes	11	3	27.3	1	9.0	27.3
Femoral-inguinal nodes	20	6	30.0	5	25.0	5.0
Retroperitoneal and mesenteric nodes	30	4	13.3	3	10.0	3.3
Mediastinal nodes	10	0	0	0	0	0
Generalized	41	1	2.4	0	0	2.4
All nodes	157	21	13.4	10	6.4	7.0
Mouth, nasopharynx and salivary glands	26	6	23.0	1	3.8	19.2
Gastrointestinal	19	6	31.5	0	0	31.5
Skin and orbit	12	3	25.0	2	16.7	8.3
Spleen and thyroid	4	0	0	0	0	0
Total	218	36	16.5	13	6.0	10.5
B—Treated Cases						
Cervical nodes	37	7	19.0	1	2.7	16.3
Axillary nodes	9	3	33.3	1	11.0	22.3
Femoral-inguinal nodes	14	5	35.7	4	28.5	7.2
Retroperitoneal and mesenteric nodes	17	3	17.7	2	12.0	5.7
Mediastinal nodes	5	0	0	0	0	0
Generalized	26	1	3.8	0	0	3.8
All nodes	108	19	17.6	8	7.0	10.6
Mouth, nasopharynx and salivary glands	21	6	30.0	1	4.7	25.3
Gastrointestinal	16	6	37.5	0	0	37.5
Skin and orbit	8	3	37.5	2	25.0	12.5
Spleen and thyroid	3	0	0	0	0	0
Total	156	34	21.8	11	7.0	14.8
C—Untreated and Unknown						
Total	62	2	3.2	2	3.2	0

All preceding studies agree that some cases of lymphosarcoma have a long, natural duration. For that reason, it would seem, the five year period of observation is not long enough to decide whether permanent cures have been effected. It is known that at least one third of the five year survivors have persisting disease, and it is argued that the rest may all eventually die of it. The present study was undertaken with this point particularly in mind.

Before I discuss our results, it seems necessary to make a statement regarding the criteria used to make the diagnosis of lymphosarcoma. Obviously this is a loose term and has never been clearly defined. Most observers today are unwilling to follow Minot and

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Read before the Bronx Pathological Society, Dec. 14, 1940, and the International Post-Graduate Medical Assembly of Southwest Texas, San Antonio, Texas, Jan. 28, 1941.

1. Minot, G. R., and Isaacs, Raphael: Lymphoblastoma (Malignant Lymphoma), J. A. M. A. **86:** 1185-1189 (April 17), 1265-1270 (April 24) 1926.

2. Desjardins, A. U.: Radiotherapy for Hodgkin's Disease and Lymphosarcoma, J. A. M. A. **99:** 1231 (Oct. 8) 1932.

3. Krumbhaar, E. B.: The Lymphomatoid Disease, J. A. M. A. **106:** 286 (Jan. 25) 1936.

4. Sugarbaker, E. D., and Craver, L. F.: Lymphosarcoma: A Study of 196 Cases with Biopsy, J. A. M. A. **115:** 17-23 (July 6), 112-117 (July 13) 1940.

5. The experience of others tends to confirm this. Jutras (Contribution à l'étude des influences anatomo-pathologiques et radiotechniques dans le traitement des sarcomes lympho-ides du pharynx par radium et rayons X, J. de radiol. et d'électrol. **19:** 425 (Aug.) 1935) of the Paris Radium Institute reported 25 per cent survivals over five years for lymphosarcoma of the pharynx.

Isaacs in merging all malignant lymphomatoses with Hodgkin's disease under the all inclusive term lymphoblastoma, and they are not expert enough in histologic methods to utilize Robb-Smith's [6] elaborate subdivision of what he chooses to call "reticulosarcoma." This is based on Maximow's hypothesis of the pluripotency of certain primitive cells of the embryonic mesenchyme, which may persist throughout life and consists of twelve

TABLE 2.—*Lymphosarcoma (1915-1930 Inclusive)*

		Survived 10+ Years		Died or Alive with Tumor 10+ Years		Symptom Free 10+ Years,
		No.	Per Cent	No.	Per Cent	Per Cent
All cases	90	8*	8.9	2†	2.2	6.7
Treated cases	48	7	14.6	1	2.1	12.5
Untreated cases	42	1	2.4	1	2.4	0

* These cases were distributed as follows: lymph nodes 4 (1 untreated); oral cavity and nasopharynx 2; stomach 2.
† These cases were primary in lymph nodes.

different names. It is a brilliant and valiant attempt to bring order into a chaotic subject, but there is need for more simplification before it can be accepted and used. My associates and I contemplate using the method of tissue culture in an investigation of the lymphomatous tumors, since it has thrown considerable light on the cellular origin of other neoplasms, but it will probably be several years before our efforts can bear fruit.

Meanwhile, those concerned with the treatment of lymphosarcoma feel the need of names that can be easily recognized and used. There are three terms commonly employed: lymphocytic cell type, reticulum cell type and giant follicle type. Evidently there is no agreement about the first two, for while Warren and Picena [7] found only 3.6 per cent reticulum cell sarcomas among 308 lymphoid tumors, Sugarbaker and Craver, no doubt guided by Ewing and Stewart, reported 94 per cent reticulum cell tumors among 196 cases. I continue to use these three terms also for convenience. Our criteria, although no doubt inexact, are very simple. We call them tumors of the lymphocytic cell type when the predominant tumor cell is small — only slightly larger than a small lymphocyte. The term reticulum cell type is applied to all lymphosarcomas whose cells are larger than this. The giant follicle tumors are characterized, as the name implies, by the formation of follicles of a size larger than is ever seen in any benign lymphomatous process. Although there is some difference of opinion as to whether this condition is a malignant tumor, the observations of Baehr,[8] and more recently of Baehr and Klemperer,[9] are convincing evidence that it is. As will be seen, our own experience coincides with theirs.

During the twenty-one year period 1915-1935 we examined a total of 218 cases of lymphosarcoma with microscopic confirmation of the diagnosis. For 156 of these patients some form of curative therapy was attempted, while for the remaining 62 either curative therapy was not given or it is unknown whether or not it was given. Ninety of these patients were seen during the sixteen year period 1915-1930, of whom 48 were treated and 42 were not. In the evaluation of results it is our feeling that all cases should be counted as failures unless their survival is known; consequently an analysis of these figures into dead, lost and not followed is omitted.

Table 1 deals with the twenty-one year period and shows the five or more year survivals so far as is known. If all the cases are included, the five year survival rate is 16.5 per cent. But since about one third of these are known to have had persisting disease at five years, the symptom-free survival rate is only 10.5 per cent. In the second and third sections of this table, the gross figures are analyzed into *B*, those who were treated with roentgen therapy, surgery or a combination of the two, and *C*, those who received no curative therapy so far as our records show. The five year survival rate for the treated group is 21.8 per cent. Again about one third of these patients are known to have had persisting disease at five years, so that the symptom-free survival rate is 14.8 per cent. Finally, the untreated group had a five year survival rate of 3.2 per cent, but none of these survivors were free from disease.

The second table shows the cases recorded during the sixteen year period 1915 through 1930, analyzed in a similar fashion. Although the percentage rates are smaller, it demonstrates that while there is a survival rate at ten years of 14.6 per cent and 2.4 per cent respectively for treated and untreated patients, it is only the treated group that has symptom-free survivors at ten years.

Further study of these two tables shows some interesting things. Statistically the five year survival rate is better than average if the disease first manifests itself in the cervical, axillary and inguinal nodes, the oral cavity and nasopharynx, the gastrointestinal tract and the skin and orbit, and poorer than average if it starts in the retroperitoneal, mesenteric or mediastinal nodes or the spleen and thyroid or is generalized. Persistence of disease and later deaths, however, narrow the more favored group to the cervical and axillary nodes, the mouth and nasopharynx and the gastrointestinal tract.

A second striking observation comes from a comparison of the treated and untreated patients. Whereas in the treated group 21.8 per cent survived five years and 14.8 per cent were symptom free, in the untreated

TABLE 3.—*Cases of Lymphosarcoma Arranged According to Histologic Type*

		5+ Year Survivals		Died or Alive with Tumor After 5 Years		Symptom Free 5+ Years,
		No.	Per Cent	No.	Per Cent	per Cent
All cases						
Reticulum cell	80	11	12.1	6	6.7	5.4
Lymphocytic cell	55	11	20.0	6	10.9	9.1
Giant follicle	20	7	35.0	3	15.0	20.0
Total	164*	29	17.7	15	9.1	8.6
Treated cases						
Reticulum cell	63	10	15.9	5	8.0	7.9
Lymphocytic cell	41	11	26.8	6	14.6	12.2
Giant follicle	17	6	35.3	2	11.8	23.5
Total	121	27	22.3	13	10.7	11.6

* In the other 54 cases either slides were no longer available or the preparations were unsatisfactory for accurate typing.

6. Robb-Smith, A. H. T.: Reticulosis and Reticulosarcoma: A Histological Classification, J. Path. & Bact. **47:** 457 (Nov.) 1938.
7. Warren, Shields, and Picena, J. P.: Reticulum Cell Sarcoma of Lymph Nodes, Am. J. Path. **17:** 385 (May) 1941.
8. Baehr, George: The Clinical and Pathological Picture of Follicular Lymphoblastoma, Tr. A. Am. Physicians **47:** 330, 1932.
9. Baehr, George, and Klemperer, Paul: Giant Follicle Lymphoblastoma, Benign Variety of Lymphosarcoma, New York State J. Med. **40:** 7 (Jan. 1) 1940.

group only 3.2 per cent survived more than five years and none were free from disease. In the older group the ten year survivors of treatment were 14.6 per cent total with 12.5 per cent symptom free, while only 1 untreated patient survived ten years before dying of the disease. It may be objected with justice that the composition of the treated and untreated groups is different and not properly comparable, but it cannot be gainsaid that there are symptom-free survivors at five and ten years in the treated groups and none in the untreated groups.

Our experience parallels that of Sugarbaker and Craver with respect to age. Of the 36 long survival cases 1 was under 20 years. This was a boy of 13 with giant follicle lymphosarcoma of the cervical nodes who was well sixty-one months after radiotherapy. Of the rest, 4 were in the third decade, 4 in the fourth and the other 27 were 40 years or older. No patient who has survived ten or more years was in the first three decades of life when first treated.

Six of our patients with lymphosarcoma died eventually with leukemia. The most interesting of these had a giant follicle lymphosarcoma of the inguinal lymph nodes treated by excision and radiotherapy. She also had a carcinoid of the appendix removed and finally died ninety-one months after excision of the inguinal nodes with lymphatic leukemia. This was the only time that I have seen giant follicle lymphosarcoma associated with leukemia.

TABLE 4.—*Type of Treatment Used in Cases of Lymphosarcoma with Long Survival*

	Number *	Per Cent
Radiotherapy alone	19 (4)	52.8
Excision and radiotherapy	8 (2)	22.2
Excision alone	7 (1)	19.4
Biobsy alone	2 (1)	5.6
Total	36 (8)	100.0

* Figures in parentheses are ten year survivals.

Sugarbaker and Craver expressed the opinion that histologic examination did not help in prognosis except in giant follicle lymphosarcoma, which has a much longer average duration of life than any other kind. Since almost all their cases were classified as reticulum cell sarcomas, this is easy to understand. Using the simple criteria already described, table 3 shows that in our cases there is a definite difference between the three types in absolute and symptom-free survival rate. The reticulum cell group had the greatest number of cases and a survival rate well below the average. Lymphocytic cell tumors are next most frequent with a survival rate about 1 percentage point above the average and the giant follicle tumors with the smallest number of cases show a survival rate about 12 percentage points above the average. I believe, therefore, that the division of the tumors into histologic groups is one factor that may be used with others in statistical prognosis.

Clinically, a majority of the lymphosarcomas seem to have a focal origin. All but 1 of our treated patients who have survived symptom free for more than five years and all of the ten year symptom-free survivors had either a single primary focus or at most two contiguous anatomic areas involved when treatment was begun. The single exception was a woman aged 28 with generalized glandular involvement by a giant follicle lymphosarcoma. She was treated with roentgen rays and remained symptom free sixty-four months after treatment. This indicates the importance of early diagnosis and is a strong argument in favor of the more frequent use of diagnostic biopsy without procrastination in cases of unexplained localized lymph node enlargements.

Table 4 shows that radiotherapy has been the most frequently used form of treatment. It was the sole form of therapy in half of the long survival cases and was combined with surgery in another quarter. But it is significant that it is possible to have long survivals following surgical removal alone. Six of these cases were symptom free when last seen. Two involved lymph nodes, 3 the gastrointestnial tract and 1 the external canthus of the eye. This suggests that the disease may sometimes remain confined to the vicinity of its focal origin for a sufficiently long time to permit its complete eradication by such a limited procedure as local excision. Finally, the table emphasizes the fact that in rare instances, even if untreated, the disease may pursue an exceedingly slow course lasting many years.

SUMMARY

This study has brought out the fact that in the group of patients observed by us, although 1 patient survived ten years without treatment before dying of lymphosarcoma, there were 7 treated patients who lived that length of time and 6 of them are symptom free. One cannot know that these 6 patients are cured but, on the other hand, it is not justifiable to assume that they are not. The great difference in favor of the treated cases over such a long period of time gives one the right to anticipate that some of these clinical cures may be absolute ones.

The favorable results have been obtained almost always while the neoplasm is still relatively localized. If more cases are recognized and treated in this early stage, the number of cases of long survival will be increased. This means the earlier biopsy of enlarged nodes and suspicious tumors in the known areas of involvement.

Probably because the disease usually has a focal origin, the long symptom-free survivals have followed both radiotherapy and surgery used either alone or in combination. Since lymphosarcoma is generally radiosensitive, roentgen therapy is usually preferred. If surgery is selected as the primary treatment it is probably better to follow it with roentgen therapy.

There are some factors that may be taken into consideration in the prognosis. Giant follicle tumors are the least malignant and reticulum cell tumors the most malignant of the lymphosarcomas. If the neoplasm manifests itself before the age of 20, the chances of long survival are minute; they are greatest if the patient has passed his fortieth year. Cases associated with leukemia are always fatal. The mouth and nasopharynx, the gastrointestinal tract and the cervical and axillary lymph nodes are more favorable sites of origin, while the spleen, the thyroid, the mediastinum, the retroperitoneal region and generalized lymph node involvement are the least favorable. If the disease has involved more than two contiguous anatomic structures, the chances of symptom-free long survival are very remote. A long survival irrespective of the degree of involvement or of treatment may be expected in between 2 and 3 per cent of all cases.

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NONSPLINTING TREATMENT OF FRACTURES OF THE ELBOW JOINT

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In the treatment of any type of fracture, the first thought that comes to mind is fixation and splinting. Concerning fractures of the elbow joint, however, equal consideration should be given to the concept of nonfixation. That a considerable degree of dysfunction has been the rule rather than the exception with splinting treatment is confirmed by Cohn.[1] He states that "end results in fracture of the elbow are not good." He and others admit that the avoidance of complications such as Volkmann's ischemic contracture, myositis ossificans or ulnar neuritis is easier than treatment of these conditions later.

Deviation from traditional treatment was tried in a series of cases because of the unsatisfactory results obtained in a case at Fort Totten in which an officer sustained a minor fracture of the elbow joint as a result of a fall during a basketball game, with resulting ankylosis and calcification.

REPORT OF CASES

CASE 1.—First Lieutenant A. A., aged 32, was roentgenographed immediately after the accident on Dec. 9, 1939 and films showed (1) simple complete fracture of the extreme tip of the right coronoid process. The multiple small fragments were in fair alinement but separated about ⅛ inch from the coronoid process itself; (2) simple incomplete fracture of the head of the right radius; the lateral margin of the head was broken into several small fragments, which were displaced toward the hand and laterally approximately ¼ inch.

The patient's arm was immobilized at 90 degrees for several weeks by means of a plaster cast. On removal of the dressings, considerable lack of motion was encountered in flexion and extension as well as in supination and pronation. Weight carrying diathermy and massage as well as passive manipulation were instituted. Roentgenograms at this time revealed rather diffuse callus formation in the vicinity of the fracture and a slight amount of calcification in the surrounding soft tissues. Manipulation under general anesthesia, treatment with hot compresses, diathermy and massage produced considerable restoration of motion, and x-ray examination showed fair position and normal callus formation in the fracture area of the coronoid. However, considerable hypertrophy and deformity of the head of the radius were noted. After the pain and swelling had subsided, the patient was encouraged to pursue his usual activities and was told to return several times weekly for further treatment. The elbow appeared to have a normal contour. Although pronation and supination developed normally, restricted motion persisted in this elbow, which prevented extension beyond 120 degrees and flexion to better than 30 degrees. At the time of the August maneuvers, about nine months later, it was noted that the arm was still unimproved.

The basis for a concept of nonsplinting treatment lies in the fact that fractures of the elbow joint itself, involving the joint surfaces, are concerned with fractured bones the fragments of which are comparatively short; and it is difficult to realine them properly for this reason with the use of external mechanical force. And it is even more difficult to hold them in realinement once such primary alinement is attained. Blauvelt [2] recognizes this problem when he states that "in no joint in the human body is such a variety of mishaps to the opposing bones possible as in the elbow. And in no part of the body skeleton are fractures followed by more disabling complications than in this region." Buchanan [3] also admits that "the uncontrollable short fragment is a problem in accurate reduction and retention. When there is a short fragment near a joint, it is not controllable by external splinting." He advises open operation, with which I do not concur.

The excellent circulation and rather extensive cartilage surface of this joint favors a tendency to ankylosis and calcification when fracture occurs. Even in cases in which the cast or external splint is removed early, achievement of the normal state and normal function is a tedious and often painful process. Since the blocking of the circulation in the joint is one of the most important things to guard against, it seems obvious that a nonfixation type of treatment would be the procedure of choice. Gould [4] thinks that complications such as Volkmann's ischemic contracture, in which there is more or less sudden transformation of muscles into dense fibrous tissue, result from interference with the venous return from the muscles, while the arterial supply remains intact. He says "The most successful treatment is prevention, and this means avoidance of circular bandages and avoidance of acute flexion in the presence of swelling." Buchanan [3] reiterates that "circulatory ease" is essential in healing and suggests that a horizontal or slightly centripetal down slope is the position which will minimize pain and prevent edema, with its vicious circle of circulatory obstruction, fibrosis, and so on. Frost [5] says "I am not so particular about complete immobilization of fractures in injuries to the elbow. In the early stage, because of the pain and swelling, the patient cooperates nicely in maintaining the injured elbow quite fixed."

In the series of cases to which this new concept of treatment was applied, no fixation was employed by external splints or casts or other measures ordinarily used for immobilization. The fracture or fractures in the vicinity of the elbow joint were maintained in the functionally flexed position by a simple triangular bandage suspended from the neck. Movement of the forearm and arm as well as of the elbow joint was encouraged as soon as possible, in keeping with the painful limits of the injury. A good deal of induration and swelling is precipitated almost immediately after such a fracture, and the application of a cast or external splint would only aggravate this condition and should, I think, be considered a dangerous procedure. Furthermore, the nonfixation treatment permits close observation of the condition of the joint and early treatment of any untoward symptoms and complications.

While many authors [6] do not consider it advisable to institute active or passive motion for several days or weeks after the injury, I have found that motion of the hand, fingers, forearm and wrist, when encouraged as soon as possible, produced a better functional result and was in line with the universal concept of functional therapy. I agree with Eliason and North,[7] however,

1. Cohn, Isidore: Personal Observations on Fractures About the Elbow, J. Oklahoma M. A. **27:** 92 (March) 1934.
2. Blauvelt, Hugh: Fractures Around the Elbow Joint, M. Press **197:** 443 (Nov. 16) 1938.
3. Buchanan, Lyle: Fractures Around the Elbow Joint, M. J. Australia **2:** 881 (Dec. 26) 1936.
4. Gould, A. L.: A Neglected Danger in the Treatment of Elbow Fractures, Maine M. J. **27:** 116 (June) 1936.
5. Frost, J. G., in discussion (p. 140) on Bendixen, P. A.: Fractures of the Elbow, Internat. J. Med. & Surg. **46:** 101 (March) 1933.
6. Higgs, S. L.: Fractures in the Region of the Elbow Joint, Brit. M. J. **2:** 230 (July 3) 1938.
7. Eliason, E. L., and North, J. P.: Fractures About the Elbow, Am. J. Surg. **44:** 88 (April) 1939. Reich, R. S.: Early Motion in Elbow Fractures, Physiotherapy Rev. **17:** 7 (Jan.-Feb.) 1937. Roberts, W. M.: Management of Elbow Fractures, South. Med. & Surg. **92:** 8 (Jan.) 1930.

that it is the voluntary, active movement of the patient, which constitutes the major element in recovery. The surgeon may guide movements; he may support the weight of the extremity, but he cannot hasten matters by forcible passive motion or stretching under anesthesia.

The important thing from the patient's point of view is to get as perfect a restoration of function as possible. The anatomic correction, as Frost [5] says, may be of great importance in the event that a compensation case goes before the industrial commission. It is interesting to note in this connection that many times roentgenograms will show that there is improper anatomic correction, but functionally the result is satisfactory. McKee [8] humorously describes his mountaineer patients having fractured elbow joints and his trials and tribulations in treating them. He describes devious types of fixing devices he has had to use. Most interesting in relation to this article are 2 cases he recounts in which, because of excessive swelling and edema, he applied no splinting apparatus. The arm was allowed to lie on a pillow at the carrying angle. In both of these cases, he reports, function is 100 per cent. McKee adds "Our results have run the cycle of recovery as truly as has our treatment; some untreated cases have regained 100 per cent function; one much treated case, a 90 per cent dysfunction."

Following is a group of cases of elbow fracture treated at Fort Totten Station Hospital by the nonsplinting methods. It has been gratifying to observe that all of these patients regained 100 per cent function:

CASE 2.—Private (first class) J. E. C., aged 22, entered the hospital by ambulance, after having sustained an injury to his left elbow July 2, 1940. He had fallen on the flexed arm while running to catch a bus. His past history was noteworthy for the fact that he had had a broken left arm fifteen years previously. The x-ray examination on admission revealed (1) a comminuted fracture of the lateral condyle with slight displacement upward, laterally and backward, extending through the lateral portion of the capitellum into the joint proper; (2) simple avulsion fracture, medial epicondyle with displacement downward and backward. The fracture was treated by placing the arm in a triangular sling. In less than a week the swelling had receded and the patient could obtain some flexion of the elbow. Two weeks later extension was estimated at two-thirds and flexion at one-half normal and the hand grip was good. On September 26 the patient could fully extend his elbow forcibly while receiving diathermy. When discharged to duty on October 25, extension was approximately 180 degrees and flexion 5 degrees without effort.

CASE 3.—Private R. F., aged 21, was admitted April 18, 1941. His elbow had been injured by a piece of coal (8 by 4 inches) which had been hurled at him by a prisoner while he was acting as guard on duty. He was unable to move his arm at the elbow, and the latter bled profusely. His past history included a broken left wrist eight years previously. The diagnosis was a transverse fracture through the base of the olecranon process of the left ulna, the fragments being in good position. The nonsplinting treatment was instituted and on April 30, 1941 the patient was discharged to duty, cured, with 100 per cent function regained.

CASE 4.—Corporal A. J. L., aged 27, admitted May 4, 1941 from command, while packing equipment prior to transfer was going down a flight of stairs and his heel caught in one of the steps. He felt himself falling and in trying to grasp hold of the side rail he missed his footing entirely and fell the remainder of the distance (about four steps), landing on his right shoulder. There was no immediate pain or discomfort, but later the patient found he could not move his right arm while attempting to put on his trousers. He reported to the hospital, where it was found that he had a simple comminuted complete fracture of the right clavicle and a simple comminuted fracture of the olecranon process of the right ulna. His progress was satisfactory on the nonfixation treatment and on June 30, 1941 he was discharged to duty with a good functional result.

CASE 5.—R. E. V., aged 22, admitted on March 26, 1940, was a laborer, transferred from a CCC camp to Fort Totten with a reset left elbow, which he had dislocated when he fell down a gully while carrying brush on March 21, 1940. His elbow was swollen; pronation and supination were normal, flexion and extension severely limited. The diagnosis was simple complete fracture of the epicondyle of the left humerus and simple complete dislocation of the left elbow. Good progress was made on the nonsplinting treatment and he was discharged cured on May 23.

CASE 6.—Private D. G. C. was admitted August 21, 1941 with a history of having injured his elbow on July 24, 1941 while going down a steep embankment; he lost his balance and fell on his arm. The doctor had told him there was nothing broken and to rest his arm. However, the elbow became swollen and discolored three days later. The soldier continued on duty to the best of his ability. He reported to the hospital for reexamination, because his hand was giving him some trouble and on x-ray examination it was found that he had a comminuted fracture through the head of the left radius with no appreciable separation of fragments. There was no evidence of any callus formation. A triangular sling was applied and excellent progress continued until discharge.

COMMENT

While the treatment of elbow fractures herein suggested may be a radical deviation from previously accepted methods, the evidence presented in connection with this new concept of therapy is worthy of consideration. Many authors have hinted at the advisability of less drastic measures (than plaster casts and open operation) in the treatment of fractures about the elbow, but none have mentioned their willingness to dispense with the old methods of splinting and other forms of fixation. In certain types of these cases Vernon [9] advocates the application of a modified triangular sling, which he describes in detail; but he mentions that it must be used cautiously and with reservation. It is my opinion that the nonfixing type of treatment in fractures of the elbow may be applied in all cases with profit and with greater restoration of normal function and should be the rule, with fixation and splinting the exception.

This method of treatment may be applied to children as well as to adults.

CONCLUSIONS

1. Since the fractured segments in fractures of the elbow are not long enough to be manipulated in reduction, the nonfixing methods should be the treatment of choice.

2. Interference with the circulation about the elbow, brought about by the application of plaster casts, tight bandages, and the like, is responsible for many of the complications and the high degree of dysfunction resulting from the fixating treatment.

3. Greater restoration of function was attained by this method in the series of cases presented.

4. The method may be used in the treatment of children as well as of adults.

8. McKee, T. K.: Fractures Around the Elbow Joint in the Hands of the General Practitioner, Virginia M. Month. **60**: 102 (May) 1933.

9. Vernon, Sidney: Modified Sling for Fractures About the Elbow, Am. J. Surg. **23**: 555 (March) 1934.

Clinical Notes, Suggestions and New Instruments

SULFADIAZINE IN LYMPHOGRANULOMA VENEREUM OPHTHALMITIS

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Infection of the eye by the virus of lymphogranuloma venereum is an unusual condition, as judged by reports in the literature. Four reports of cases are reviewed by Curth and his associates,[1] who add 1 case which was first presented by Hopkins;[2] this was a case of chronic involvement, with loss of vision, which was cured by the administration of sulfanilamide.

In this paper a case of acute involvement is presented in which treatment by administration of sulfadiazine was successful, with no sequelae.

B., a man aged 40, a laboratory worker previously in good health and with no history of lymphogranuloma venereum,

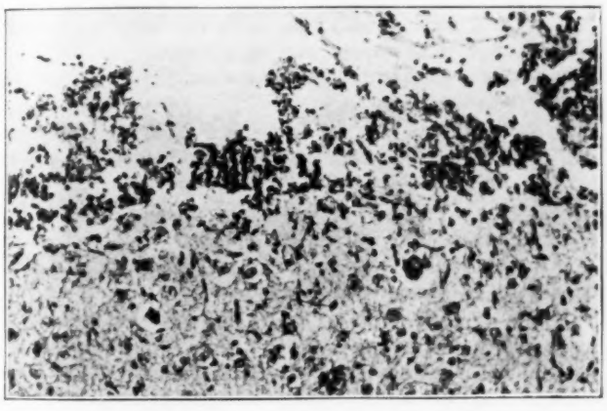

Fig. 1.—Section of mouse brain showing inflammatory reaction in fourth ventricle; × 140.

first noticed an irritation of the left eye about March 7, 1941. The complaints were a feeling of "sand under the lids" and watering of the eye. There was moderate injection of the conjunctival vessels. The condition was regarded as a simple conjunctivitis and was treated by washing occasionally with boric acid solution. The inflammatory condition slowly increased in severity and a mucoid discharge of the eye began to appear. The patient was referred to an oculist on March 20. Examination at that time showed vision of 20/20 in each eye and conjunctivitis of the left eye of moderate severity. The lids on eversion showed more congestion than the bulbar conjunctiva and presented many bleblike papules which suggested the possibility of trachoma. Slit lamp examination showed the aqueous humor to be clear and the vessels at the limbus not penetrating the cornea. Smears of the conjunctival scrapings were made but no organisms were found.

Treatment at first consisted of hot boric acid compresses every two hours and azosulfamide drops in the culdesac three times a day; dark glasses were worn and use of the eyes was restricted. The patient was observed every few days. On March 31, since there was no appreciable change for the better, the azosulfamide was discontinued and 0.2 per cent zinc sulfate 1 drop three times a day substituted.

On April 2 slit lamp examination revealed a beginning keratitis, with a few keratotic precipitates near the limbus. A search for foci of infection, including roentgenograms of the teeth

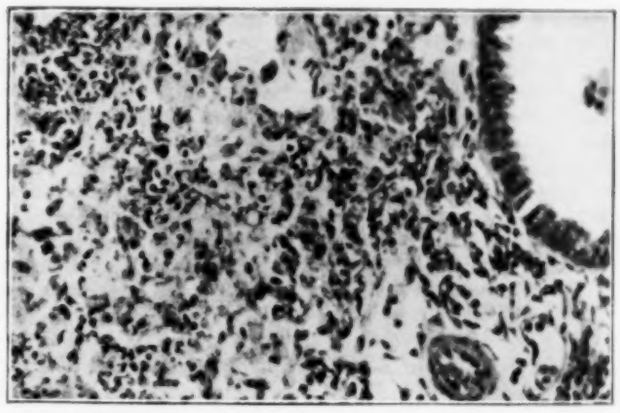

Fig. 2.—Section of mouse lung, pneumonic area; × 285.

and sinuses, examinations of the urine and prostate and a general medical check revealed nothing of positive significance. A course of intramuscular foreign protein therapy was begun. On April 4 the keratitis seemed slightly worse and a small marginal corneal ulcer at 12 on the clock dial had developed.

At this time, since the condition had gradually increased in severity in spite of continued therapy and owing to the absence of definite bacteriologic findings, it was considered that the patient might have been infected with some virus with which he had had contact in the laboratory. The virus of lymphogranuloma venereum seemed most probable, and mice were inoculated intracranially with a washing of physiologic solution of sodium chloride of the eye on April 4. The patient was then given a mydriatic and treatment was continued.

The inoculated animals remained apparently healthy until April 17, when 3 of the 5 inoculated showed signs suggestive of infection with the virus of lymphogranuloma venereum such as humping of the back, rough coat, lethargy, ataxia and slight ocular discharge.

When it seemed that the diagnosis was established, therapy was begun, on April 17, with sulfadiazine (Lederle), which had previously been found effective against the experimental infection in mice. The dose was 1 Gm. by mouth three times a

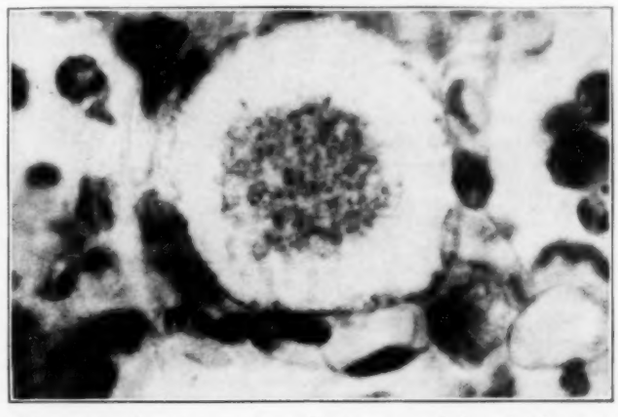

Fig. 3.—Section of mouse lung showing accumulation of "elementary bodies" in a vacuole in pneumonic area; × 1,500.

day after meals. Up to the time this treatment was begun the condition of the eye had shown no change for the better, but after treatment with sulfadiazine there was a definite, progressive improvement until April 28, at which time the eye was perfectly clear (vision 20/20) and the patient was discharged from treatment. He had received 1 Gm. of sulfadiazine three

From the Division of Infectious Diseases and the Division of Pathology of the National Institute of Health, Bethesda, Md., and the Relief Station, Washington, D. C.

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2. Hopkins, J. G.: Chronic Conjunctivitis of the Right Eye, Probably Due to the Virus of Lymphogranuloma Venereum, Arch. Dermat. & Syph. **39**: 742 (April) 1939.

times a day for five days, followed by a rest period of three days, at the end of which time a second course of the drug was started. In all, 30 Gm. was given. Recovery was considered complete on April 28, ten days after this therapy was first begun.

Following recovery a Frei test was done and the reaction was interpreted as positive; a wheal 8 mm. in diameter, surrounded by an area of erythema, developed. The reaction did not subside completely until about ten days later. Serum was also obtained and a complement fixation test was done by Dr. G. W. Rake of the Squibb Institute, who reported positive complement fixation in a serum dilution of 1:60, which was the highest dilution tested.

The virus was maintained without difficulty by serial passage of infected mouse brains at three to four day intervals; it was also adapted to mouse lung by intranasal inoculation of an emulsion of infected brain in physiologic solution of sodium chloride, resulting in an extensive fatal pneumonia. Examinations of tissue sections showed brain lesions apparently consistent with those reported by Findlay [3] and seemingly identical with those found previously in this laboratory in studies of two different strains of virus of lymphogranuloma venereum. The pulmonary lesions appeared to be the same as those reported by Shaffer, Rake and McKee [4] as characteristic of this virus.

SUMMARY

A patient with probable accidental infection of the eye with the virus of lymphogranuloma venereum was successfully treated by the administration of sulfadiazine.

THROMBOPENIC PURPURA DUE TO SULFATHIAZOLE

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Thrombopenic purpura has been observed and described as a manifestation of drug toxicity during the administration of sulfanilamide [1] and of sulfapyridine.[2] It has yet not been reported with the use of sulfathiazole. The following case is one in which this complication occurred.

REPORT OF CASE

History.—A carpenter aged 37 was admitted to the Jewish Hospital Sept. 11, 1941. He had experienced left renal colic seventeen years before and a calculus was removed from the urinary bladder by cystoscopy. Three years later a similar episode occurred. The patient then experienced good health until one year before admission, at which time he again had left renal colic. A nephrostomy was performed at another hospital but the patient did not know whether a calculus was removed. The wound healed and the patient was comfortable for the next three months. For nine months prior to admission he had frequent attacks of pain in the left flank, becoming severe three days before admission and radiating to the back. In addition, he had fever and frequency of urination with dysuria and pyuria.

The family history was irrelevant. In the past history the occurrence of scarlet fever and two operations for hernia were noted. There was no history of venereal disease. He never had hemorrhagic manifestations. He had taken plenty of orange juice in his daily dietary.

Physical Examination.—On admission the temperature was 104.4 F., the pulse rate 90 and the respiratory rate 30. The skin and the mucous membranes appeared normal. The heart and lungs were normal. The systolic and diastolic pressures were 110 mm. and 60 mm. of mercury respectively. Abdominal examination showed a definitely tender mass in the left flank (presumably kidney), moving freely with respiration. There was severe left costovertebral tenderness. The edge of the liver was felt two fingerbreadths below the right costal margin. The spleen was not felt. The prostate gland was not enlarged or tender.

Laboratory Studies.—A catheterized specimen of urine on admission was normal microscopically and tests for albumin and sugar gave negative results. Culture yielded Proteus vulgaris. The blood urea was 16.5 mg. per hundred cubic centimeters and five days later it was 9.8 mg.; blood uric acid was 4 mg., calcium 8 mg., phosphorus 3.5 mg. and phosphatase 2.4 units per hundred cubic centimeters. The Kline test gave negative results. Blood culture was sterile. An intravenous phenolsulfonphthalein test showed 37.5 per cent of dye recovered after one and one-half hours. Intravenous urography revealed that the right kidney functioned normally. In the left ureter was a large calculus just above the ureterovesical junction measuring about 3 cm. in its long diameter. The left kidney appeared larger than the right but failed to excrete the medium.

The blood count on admission was hemoglobin 90 per cent (Haden-Hausser), erythrocytes 4,700,000 and white blood cells 14,000 per cubic millimeter. The blood smears showed 71 per cent segmented and 13 per cent nonsegmented polymorphonuclear neutrophils, 15 per cent lymphocytes and 1 per cent monocytes. Platelets were abundant. The red blood cells showed no abnormalities.

Clinical Impression.—The impression was that there was a left ureteral calculus with ureteral obstruction and pyelonephritis.

Treatment.—The patient was given vitamin capsules (containing vitamins A, B_1, B_2, C and D). Sulfathiazole was administered as follows: 1 Gm. on September 11, 4 Gm. on September 12 and 0.5 Gm. on September 13.

Course.—On September 12 it was noted that the patient's temperature was declining, falling from 105 F. to 100.5 F. On September 13, after the amount of sulfathiazole reached a total of 5.5 Gm., a hemorrhagic state began to develop and the temperature rose to 103 F. He had profuse bleeding from the nose and gums, and hematuria was noted. Numerous hemorrhagic vesicles varying in size up to 1 cm. in diameter appeared on the tongue, lips and buccal mucosa. There was also an extensive petechiasis of the skin and mucous membranes. Extreme pallor developed. The spleen was not palpable and there was no enlargement of the lymph nodes. A blood study showed hemoglobin 50 per cent (Haden-Hausser), red blood cells 2,600,000, white blood cells 12,400 and platelets 2,000 per cubic millimeter respectively. The differential leukocyte count was 57 per cent segmented and 18 per cent nonsegmented polymorphonuclear neutrophils, 10 per cent lymphocytes and 15 per cent monocytes. There was a moderate degree of anisocytosis, poikilocytosis, and polychromatophilia and a slight degree of macrocytosis and microcytosis. Reticulation was 3 per cent. The smears showed an absence of platelets. The bleeding time was six minutes and the coagulation time four minutes. The tourniquet test was strongly positive. Clot retraction time was not done. Sternal puncture revealed 3 per cent myeloblasts, 33 per cent neutrophilic myelocytes, 1 per cent eosinophilic myelocytes, 21 per cent metamyelocytes, 30 per cent nonsegmented and 12 per cent segmented polymorphonuclear neutrophils. Two plasma cells were seen per hundred myeloid leukocytes. The granulocyte-nucleated erythrocyte ratio was 70:30, indicative of an increased erythrogenesis. The erythroblast-normoblast ratio was 30:70, indicative of a moderate delay in maturation. The megakaryocytes were present in goodly number and showed degenerative changes.

3. Findlay, G. M.: Experiments on the Transmission of the Virus of Climatic Bubo to Animals, Tr. Roy. Soc. Trop. Med. & Hyg. **27**: 35-66 (June) 1933.

4. Shaffer, M. F.; Rake, Geoffrey, and McKee, Clara M.: Agent of Lymphogranuloma Venereum in the Lungs of Mice, Proc. Soc. Exper. Biol. & Med. **44**: 408 (June) 1940.

From the Department of Laboratories, Division of Hematology, and the Department of Urology of the Jewish Hospital.

1. Hageman, P. O., and Blake, F. G.: Clinical Experience with Sulfanilamide in the Treatment of Beta Hemolytic Streptococcic Infections, Am. J. M. Sc. **195**: 163 (Feb.) 1938. Chemotherapy for Infectious Diseases and Other Infections (Table of Manifestations of Toxicity), Circular Letter No. 81, J. A. M. A. **116**: 513 (Feb. 8) 1941.

2. Russell, H. K., and Page, R. C.: Thrombocytopenic Purpura Due to Sulfapyridine, Am. J. M. Sc. **200**: 495 (Oct.) 1940. Chemotherapy for Infectious Diseases and Other Infections.

Sulfathiazole was discontinued on September 13 at the first appearance of the bleeding. The vitamin therapy was continued and fluids were forced. By September 16 the hemorrhagic phenomena were noted to be waning and the temperature was approaching normal. By September 18 the hemorrhagic vesicles in the mouth and the petechiae of the skin and mucous membranes had entirely cleared and the temperature and pulse had become normal. Blood smears showed the return of platelets in abundance. The bleeding time was less than one minute and the tourniquet test became negative. The hematuria, however, persisted, there being noted the continued presence of red blood cells microscopically. Because of the anemia blood transfusions were given on September 18, September 21 and September 24.

Subsequent Course.—On September 27 a uretrocystolithectomy was performed and a large calculus was removed. The following day, for prophylactic reasons, the administration of sulfathiazole was started again in doses of 1 Gm. three times a day. A total of 15 Gm. was given in five days. There was no recurrence of the thrombopenic episode. On October 3 a blood study showed hemoglobin 74 per cent, 3,600,000 red cells, 9,000 white cells. Platelets numbered 300,000 per cubic millimeter and appeared in abundance in the blood smears. The differential count was 50 per cent segmented and 5 per cent nonsegmented polymorphonuclear neutrophils, 3 per cent eosinophils, 35 per cent lymphocytes and 7 per cent monocytes. The bleeding time was thirty seconds and the tourniquet test gave negative results.

COMMENT

The patient experienced a severe thrombopenic hemorrhagic state during the administration of sulfathiazole. Although the dose was not large (5.5 Gm. over a period of three days), there was no other likely apparent cause for the purpura. There was no history of vitamin C deficiency, and the purpura occurred during adequate administration of vitamin C. There was no uremia. Blood culture ruled out bacteremia. Studies of the blood and bone marrow showed no primary blood dyscrasia. Purpura as the result of a severe intoxication caused by an infection of the urinary tract cannot be absolutely ruled out. However, the toxic state existed before sulfathiazole therapy, and the purpura appeared only after the drug was given.

It should be noted that resumption of the chemotherapy did not cause a recurrence of the purpura. Such an experience is not unusual. Long and Bliss [3] cite 2 instances and quote a third of acute agranulocytosis resulting from the administration of sulfanilamide and sulfapyridine in which readministration of the respective drugs failed to reproduce the condition. Failure to reproduce toxic effects on resumption of chemotherapy is also reported with drugs other than the sulfonamides, e. g. mapharsen.[4]

CONCLUSION

The case of thrombopenic purpura described apparently was the result of sulfathiazole medication and seems to be the first of this type due to sulfathiazole to be reported.

NOTE.—Since this report was submitted for publication, our attention has been called to the mention by Kracke [5] of a case of severe platelet depression, apparently the result of sulfathiazole medication. Purpuric symptoms were not mentioned in this case. There has also appeared the report by Quick and Lord [6] of a case of acute hemolytic anemia following sulfathiazole administration. In the latter case a purpuric rash was observed, the bleeding time was found prolonged, and the tourniquet test was positive. However, thrombopenia was not reported.

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3. Long, P. H., and Bliss, Eleanor A.: The Clinical and Experimental Use of Sulfanilamide, Sulfapyridine and Allied Compounds, New York, Macmillan Company, 1939, p. 284.
4. Rein, C. R., and Wise, Fred: Mapharsen in Treatment of Syphilis in Office Practice, J. A. M. A. **113:** 1946 (Nov. 25) 1939.
5. Kracke, Roy R.: Diseases of the Blood and Atlas of Hematology, ed. 2, Philadelphia, J. B. Lippincott Company, 1941 p. 443.
6. Quick, E. D., and Lord, F. D.: Acute Hemolytic Anemia Following Sulfathiazole Administration, J. A. M. A. **117:** 1704 (Nov. 15) 1941.

TOXIC EFFECT OF SULFANILAMIDE ON THE HEMOPOIETIC ORGANS IN A CASE OF POLYCYTHEMIA VERA

LOUIS GREENWALD, M.D.; JOSEPH LITWINS, M.D., AND JESS B. SPIELHOLZ, M.D., NEW YORK

An extensive literature has accumulated [1] reporting the toxic effects of sulfanilamide on the blood forming organs. These reactions consist of acute hemolytic anemia with leukocytosis, occasionally a leukemoid blood picture,[2] severe leukopenia with granulocytopenia and thrombopenia with hemorrhagic phenomena. Such deviations may occur singly or in combination. The outcome occasionally has been fatal.[3] The cases reported up to the present time usually have presented initially a normal hemoglobin and red cell count or slightly diminished values. A careful search of the literature fails to disclose any reference to a case of polycythemia vera in which there was a toxic reaction of the blood in the course of the administration of sulfanilamide. The following is the report of a case of polycythemia vera and prostatic infection in which anemia, severe leukopenia and neutropenia developed as the result of the administration of sulfanilamide.

TABLE 1.—*Peripheral Blood Studies from the Onset of Illness and After Recovery*

Date, 1940	Hemoglobin	Red Blood Cells	Leukocytes	Staff Cells	Segmented Cells	Lymphocytes	Monocytes	Eosinophils	Basophils
2/19	110	5,240	17,400	17	64	19	..	..	..
3/ 6	90	.....	7,000	4	51	42	3	..	..
3/ 9	67	3,380	1,600	..	7	93	..	..	..
3/10	70	3,700	3,400	..	..	93	7	..	..
3/11	..	.....	4,000	3	..	91	6	..	..
3/15	88	3,920	23,300	..	85	15	..	..	..
3/28	89	4,200	14,400	..	81	19	..	..	..
4/ 9	72	3,690	19,000	..	83	17	..	..	..
4/11	64	3,190	.....	..	..	..	..	..	..
4/16	82	4,160	.....	..	..	..	..	..	..
10/ 4	104	6,000	10,000	1	66	22	8	2	1

TABLE 2.—*Bone Marrow Studies on March 9 and on October 4*

On March 9, during the agranulocytic phase, total count 4,000; showed marked hypoplasia with normal erythrogenesis, maturation arrest of granulocytes at metamyelocytic stage

		Bone Marrow Recovery										
Date	Total Count	Myeloblast	Promyelocytes	Neutrophilic Myelocytes	Eosinophilic Myelocytes	Metamyelocytes	Nonsegmented Cells	Segmented Cells	Lymphocytes	Monocytes	Eosinophils	Normoblasts Per 100 White Blood Cells
10/4	84,800	1	5	11	4	23	17	28	3	..	8	43

A white man aged 61, born in Germany, the owner and manager of a cold storage establishment, was first seen by one of us (J. L.) in 1937. His chief complaints were headaches and vertigo. The patient was obese and of the plethoric type; he had considerable congestion of the conjunctivas and the characteristic plum red color of the buccal mucosa. The heart and lungs were normal. The blood pressure ranged between 160 and 180 systolic and 90 diastolic. The liver and spleen

Read before a meeting of the Graduate Fortnight at the New York Medical College, Flower and Fifth Avenue Hospitals in October 1940.

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2. Harvey, A. M., and Janeway, C. A.: Development of Acute Hemolytic Anemia During the Administration of Sulfanilamide, J. A. M. A. **109:** 12 (July 3) 1937.
3. Shecket, H. A., and Price, A. E.: Fatal Granulocytopenia Following Administration of Sulfanilamide, J. A. M. A. **112:** 823 (March 4) 1939.

were not palpable. The neurologic examination was negative. A blood count showed hemoglobin 125 per cent, red blood cells 6,700,000, white blood cells 12,000; differential count normal, cell volume 54 per cent and blood volume 120 cc. per kilogram of body weight. A diagnosis of polycythemia vera was made; he was put on a meat-free diet, phlebotomy was occasionally done and the patient obtained symptomatic relief.

In 1938 the patient had a typical attack of coronary thrombosis with positive electrocardiographic tracings. He was confined to bed for six weeks, after which he remained comfortable until the onset of his present illness. On Feb. 18, 1940, he complained of sore throat, his temperature was 103 F. for one day and there was evidence of pharyngitis. Fever recurred five days later and was intermittent for two days. Rectal examination disclosed a tender fluctuating left lobe of the prostate. A diagnosis of prostatic abscess was made. The patient appeared to be acutely ill and was hospitalized. On admission the blood count showed hemoglobin 110 per cent, red blood cells 5,240,000 and white blood cells 17,400 with 81 per cent neutrophils. For the first time urinalysis revealed sugar four plus. On February 26 the patient was found to be in uremia with a blood nonprotein nitrogen of 90 mg. A retention catheter was introduced and intravenous saline infusion given, with considerable improvement. Because of fever, ranging between 101 and 102 F., and the presence of large amounts of pus in the urine, sulfanilamide was administered. In all 33 Gm. was given by mouth and clysis between February 28 and March 6, during which time the temperature continued to fluctuate. On March 6, the hemoglobin level dropped to 90 per cent, and the white blood cell count was 7,000 with 60 per cent neutrophils. On March 9 there was a sudden rise in temperature to 104 F. with a blood count of hemoglobin 67 per cent,

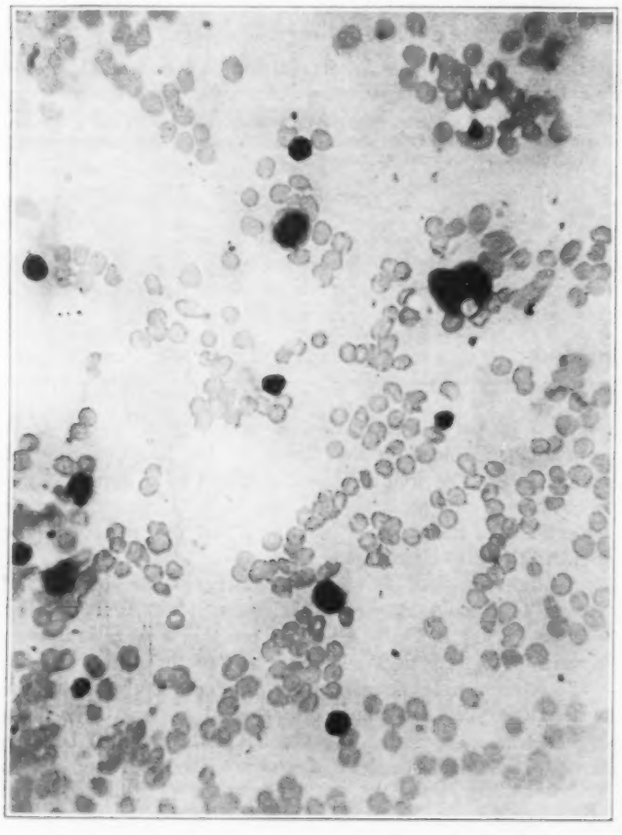

Fig. 1.—Bone marrow in the leukopenic phase, showing aplasia and absence of granulocytes beyond the metamyelocytic stage.

red blood cells 3,390,000; white blood cells 1,600, and 93 per cent lymphocytes. Chemotherapy was discontinued immediately. Aspiration of sternal marrow was done at this time. The total count of marrow material was 4,000 per cubic millimeter. The patient was given two transfusions and intravenous dextrose, with gradual improvement in the blood picture (tables 1 and 2). Following this, his general condition improved, but his urinary symptoms persisted.

Because of dysuria and urinary retention it was deemed advisable to do a prostatectomy. On March 26, suprapubic

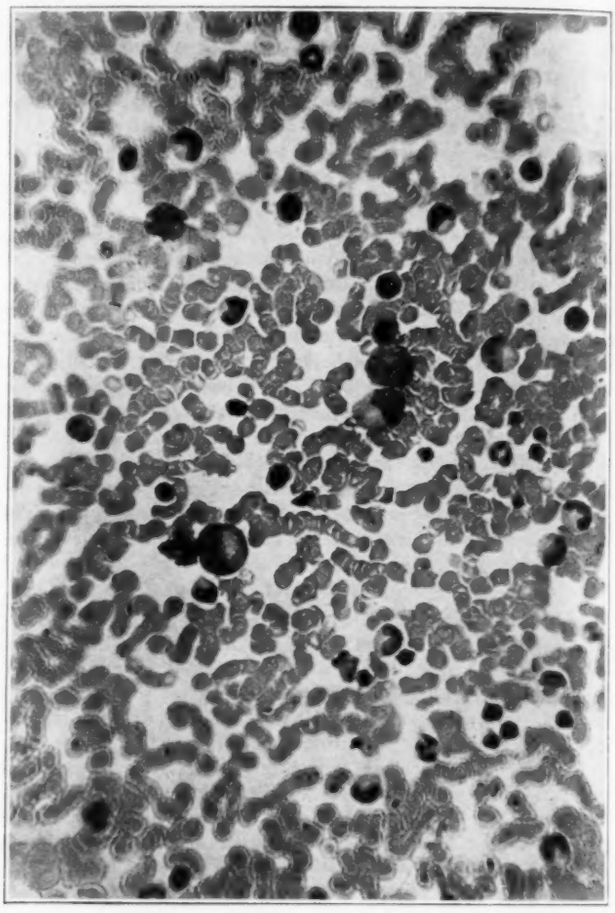

Fig. 2.—Bone marrow after recovery, showing granulocytes in all stages of development.

cystotomy and vasectomy was done. On April 2 the second stage of the operation was performed. Pathologic examination of the prostate showed the presence of an abscess in the left lobe. The patient made an uneventful recovery. Postoperatively leukocytes numbered 19,000 with 83 per cent granulocytes. However, the hemoglobin level dropped to 64 per cent and the red blood cells to 3,190,000, and it was thought advisable, because of failure to respond to iron therapy, to give a blood transfusion of 500 cc. The hemoglobin level then rose to 82 per cent and the red blood cells to 4,160,000. The patient was discharged nine weeks after admission. Blood and bone marrow studies six months later showed a return to high levels.

COMMENT

This case illustrates the importance of making frequent blood counts during the administration of the sulfonamide drugs, in spite of the presence of polycythemia. Although the anemia in this case was not as severe as may be seen in cases in which there is initially a normal count, there was a decline of the level of hemoglobin from 110 to 67 per cent and of the red blood cells from 5,240,000 to 3,700,000. There was also severe leukopenia (1,600 leukocytes with 93 per cent lymphocytes). The bone marrow at this stage was aplastic, with a complete maturation arrest at the metamyelocytic stage (fig. 1); such a condition of the bone marrow usually forebodes a bad prognosis. Here, fortunately, both the anemia and the granulocytopenia responded to transfusion. After recovery the peripheral blood counts returned to the original high values and the bone marrow showed its usual cellularity (fig. 2).

The high degree of lability of the bone marrow, and the occurrence of aplasia resulting from infections, allergic reactions, infiltrations and drugs is well known. It would be interesting to speculate, in this case, whether the hyperplastic marrow of a polycythemic patient possesses an unusual reserve for hemopoietic activity. Perhaps this offered a greater margin of safety and greater recuperative powers of the bone marrow from toxic effects following the administration of the sulfanilamide. This does not hold true in the rapidly developing anemia in polycythemia vera following the administration of phenylhydrazine. Here of course the accumulative action of the drug is also of prime importance. It will be interesting to note the effects of the sulfonamides on more patients with polycythemia and infection. The treatment that seems to give the best results is blood transfusion to correct both the anemia and the leukopenia.

SUMMARY

A patient with polycythemia vera had toxic reactions from sulfanilamide on the bone marrow and peripheral blood, with anemia, severe leukopenia and neutropenia. In spite of the severe aplasia of the bone marrow and the peripheral blood picture of agranulocytosis, recovery followed blood transfusions.

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MORBILLIFORM ERUPTION FOLLOWING USE OF SULFAGUANIDINE

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The occurrence of dermatitis following sulfaguanidine therapy has apparently not yet been recorded. This report deals with a patient who had a generalized morbilliform eruption which appeared about sixteen days after the institution of sulfaguanidine therapy but who had previously been treated with sulfanilamide, sulfathiazole and sulfadiazine without cutaneous complications.

REPORT OF CASE

A white woman aged 40 was first seen on Jan. 21, 1941 at which time a diagnosis of nonspecific ulcerative colitis was made. One week later she was sent to the Mount Sinai Hospital where 1 Gm. of sulfathiazole in suspension was given every four hours by rectum. After a total of 42 Gm. had been administered there was only a trace of sulfathiazole in each 100 cc. of blood. The patient, however, made a good temporary recovery, as evidenced by the clinical course and sigmoidoscopic studies. Because of a recurrence of the colitis, the

Fig. 1.—Appearance of cutaneous eruption of forearm.

patient reentered the Mount Sinai Hospital on April 28. During this admission the patient received 50 Gm. of sulfathiazole in suspension by rectum. Because of the persistence of the hemorrhagic, edematous and granular appearance in the lowest 5 cm. of the terminal bowel, 100 cc. of 1 per cent aqueous solution of sulfanilamide was administered rectally every six hours for a period of four days. The concentration of sulfanilamide in the blood varied from 2.4 to 4.3 mg. per hundred cubic centimeters. Sulfathiazole 4 Gm. daily was subsequently given orally for a period of eight days (May 17 to May 24). During this time the hemoglobin values dropped from 90 to 70 per cent

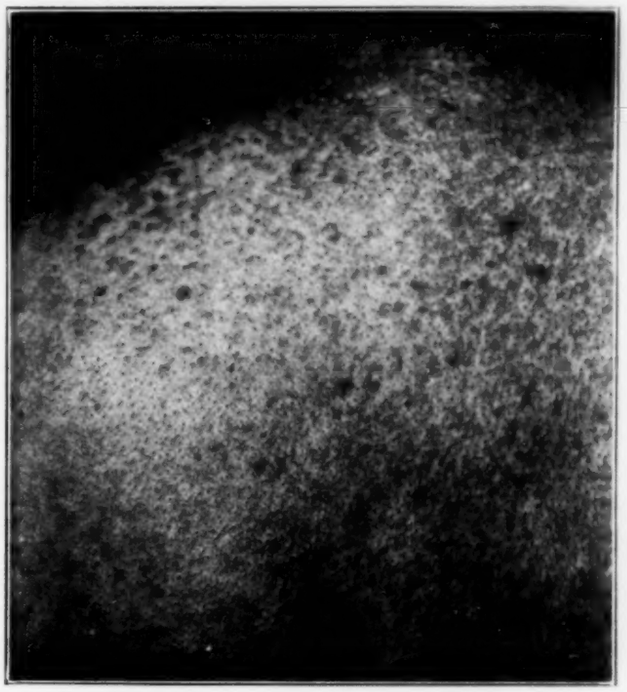


Fig. 2.—Appearance of lesions on back.

(Sahli). No other deleterious effects had been noted as a result of the chemotherapy. From June 21 to July 8 the patient was given sulfadiazine tablets,[1] 0.5 Gm. each, five times daily without any untoward effects. Because of mild recurrence of bleeding and diarrhea on August 11, sulfaguanidine 3 Gm. daily was given orally for seven days, after which time the dose was increased to 4 Gm. daily and was continued until August 27 (a period of sixteen days). At this time a temperature of 101 F. and a "measly rash" developed. Examination revealed a macular eruption resembling measles and involving the entire body except the face. The dermatitis was most severe on the abdomen, chest, back and forearms (figs. 1 and 2). The lesions varied in size from 2 to 10 mm., were pink to rose, dry, nonscaly and noninfiltrating; they were either not elevated or imperceptibly raised and disappeared on pressure. The rash disappeared within five to six days after the discontinuance of sulfaguanidine.

COMMENT

The occurrence of a dermatitis following sulfaguanidine therapy is of interest because the patient had received other sulfonamides previously without the precipitation of a cutaneous complication. The influence of sunlight can be ruled out because the patient was asked to avoid exposure to the sun's rays whenever the sulfonamides had been prescribed and because the eruption was generalized. The character of the rash herein described resembled the morbilliform toxicoderma occurring after the administration of the sulfonamides and other drugs. The conjunctivas and scleras of our patient were uninvolved.

SUMMARY

In the instance of morbilliform eruption following sulfaguanidine therapy here reported the cutaneous complication did not follow administration of sulfanilamide, sulfathiazole or sulfadiazine, which had been given prior to the institution of sulfaguanidine therapy.

876 Park Avenue—180 East Seventy-Ninth Street.

1. Supplied by Dr. D. A. Bryce, Lederle Laboratories, Inc.

Council on Physical Therapy

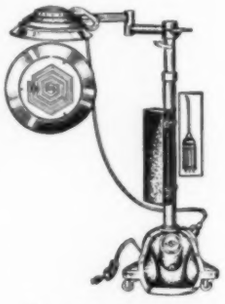
THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

ALOE COLD RAY QUARTZ LAMPS MASTER MODEL AND STANDARD MODEL ACCEPTABLE

Manufacturer: A. S. Aloe Company, St. Louis.

The Aloe Cold Ray Quartz Lamps, Master and Standard Models, are said by the manufacturer to be essentially the same with respect to electrical and radiation characteristics as the Council accepted Aloe Improved Cold Ray Quartz Lamps.[1] The firm states that:

> The changes are entirely mechanical. Both lamps have been provided with an articulated horizontal support and the Standard Model is now provided with an automatic timer. Both lamps are much heavier to protect them against the possibility of tipping and they are therefore considerably more substantial than the previous models.



Aloe Cold Ray Quartz Lamp, Standard Model.

The Master Model is recommended by the manufacturer as a large, heavy duty lamp. Its grid is 80 inches long and may be removed for hand application. An elbow type horizontal support for the burner and reflector is incorporated.

The Standard Model is smaller and has a 60 inch grid. It too is provided with the elbow type support for the burner and reflector.

In the Council's examination of the lamps it was found that they are essentially the same as the Council accepted Aloe Lamps of the same type except for the changes in design. The advertising presented by the manufacturer appears to be unobjectionable.

The Council voted to accept the Aloe Cold Ray Quartz Lamps, Master and Standard Models, for inclusion in its list of accepted devices.

FILTRO-VAPOR NASAL FILTERS NOT ACCEPTABLE

Manufacturer: Medical Products Institute, Inc., P. O. Box 1399, Cincinnati.

The Filtro-Vapor Nasal Filters are said in the manufacturer's advertising to provide "A Scientific Treatment for Common Colds . . . Also can be Used for Sore Throat, Bronchitis, Grippe, Sinus Infections." The Council secured and clinically investigated one of the Filtro-Vapor treatment sets. It was found that although the apparatus is sold by the Medical Products Institute, Inc., of Cincinnati, the same address, P. O. Box 1399, as the Allergy Research Institute is given. The prospective purchaser of the product is urged to buy both the Hayrin and the Filtro-Vapor Nasal Filter. Yet the filtering devices were identical except that the latter does not have "sterling" stamped on it.

The Filtro-Vapor Filter consists of frames (of a baser metal) structurally identical with the Hayrin filter, filtering pads and Filtro-Vapor Nasal Filter pad fluid (camphor, eucalyptus, menthol, oil of peppermint, oil of pine needles and oil of ricinoleum). The solution used on the nasal pads is claimed to be an effective form of treatment for colds and for the prevention of spread of the infection to others. In addition, the outfit contains a tube of eighteen tablets composed of acetylsalicylic acid, acetophenetidin and caffeine to be used by the sufferer if he has systemic symptoms from his colds or "grip."

The claims in the printed matter and in the correspondence are very misleading and unjustified. Following are typical examples: "This outstanding contribution to the treatment of colds, sinus, sore throat, bronchitis and grippe"; "Nasal filters act as a substitute nose until the normal functions are regained."

The referee recommends that the Council reject the Filtro-Vapor Nasal Filters for inclusion on its list of accepted devices because it is marketed under misleading claims, and because the self diagnosis and self treatment advocated by the firm favor the neglect of possibly serious disease.

1. Report of acceptance, J. A. M. A. **110:** 128 (Jan. 8) 1938.

AMERICAN RESPIRATOR ACCEPTABLE

Manufacturer: Scientific Equipment Corporation, 21 North Loomis Street, Chicago.

Distributor: American Hospital Supply Corporation, the Mechandise Mart, Chicago.

The American Respirator produces artificial respiration simulating natural breathing for indefinite periods of time. The apparatus weighs about 500 pounds and is designed for easy handling and transportation by trailer or light truck. The overall length of the unit is 72 inches and the height 54 inches; the width at the base is 26 inches, and the cylinder is 70 inches long by 30 inches in diameter.

Hinged on one side, the patient chamber opens the full length of the bed and will accommodate patients up to 6 feet 5 inches in height. The mattress is 26 inches wide and has a removable center section. Six portholes and one bed pan door permit attention to the patient's needs; the interior is visible through a full length window in the top of the chamber. The welded steel frame, mounted on swivel casters, is so constructed that the apparatus may be adjusted to the Trendelenburg position or its reverse.

Mechanical parts are concealed. Located on the control panel are large hand wheels controlling vacuum and pressure, a compound gage for recording vacuum and pressure, a hand wheel for regulating the respiratory cycle, and the motor switch. The respiratory regulation range is from 12 to 30 respirations per minute. A motor having standardized parts drives the bellows, made of rubber. In the event of power failure the unit may be operated by a hand pump.

American Respirator.

In operation the rubber collar is placed on the patient's neck and the patient is lifted into the chamber. The cover is then closed and adjustment of four metal closure catches and the closure bar seals the patient's body within the apparatus. A large screw under the head rest raises or lowers the mattress, and a hand wheel at the foot end adjusts the position of the apparatus.

In its clinical investigation the Council found the apparatus to function well mechanically. The fact that the patient chamber opens the full length of the device, and the further fact that there is no sliding bed to pull from the cylinder head, make it possible for the respirator to be used in a small space.

The Council voted to accept the American Respirator for inclusion on its list of accepted devices.

MEARS AUROPHONE, MODEL NO. 98, ACCEPTABLE

Manufacturer: Mears Radio Hearing Device Corporation, 1 West Thirty-Fourth Street, New York.

The Mears Aurophone, Model No. 98, is of the vacuum tube type.

The dimensions and weights of the various parts are as follows:

Microphone and amplifier unit, Serial No. 7883.

Circular disk shape, 3 inches diameter by 1 inch thick, weight 4.3 ounces.

Battery case with A and B batteries, 4⅝ by 2⅝ by 1½ inches, weight 12 ounces.

Crystal receiver, 1 inch diameter by 3/16 inch thick.

Batteries: The A battery was a flashlight battery No. 1050, 1½ volts. The measured A current with instrument turned full on was 31 milliamperes. The B battery was a W-20, 30 volts, and showed a current drain of 0.35 to 0.40 milliampere. A and B batteries are assembled by means of a spring clip connection to form a single unit carried in soft leather case.

Internal Noise.—With fitted ear mold the instrument could be turned up to full volume without giving feed-back squeal. The noise due to light impact on the microphone case and to rubbing of the connecting cords was not excessive.

Mears Aurophone, Model No. 98.

Acoustical Gain.—The following figures give the order of magnitude of the increase in sound level intensity at the ear of the subject over those at the microphone under conditions of actual use, as shown by audiometric measurements. They are not the same as the electrical amplification shown by measurements of electrical input and output:

Frequency	128-256	512-2,048	4,096
Volume setting full on.....	Nil	23 to 39	11 decibels

Articulation.—The usual syllable and sentence lists were used with hard of hearing subjects at a distance of 5 feet in a quiet room with the instrument set for comfortable hearing. The articulation tests showed satisfactory results.

The Council voted to accept the Mears Aurophone, Model No. 98, for inclusion on its list of accepted devices.

Council on Pharmacy and Chemistry

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. AUSTIN E. SMITH, M.D., Acting Secretary.

ALCOHOLIC ELIXIRS OF THIAMINE HYDROCHLORIDE NOT ACCEPTABLE FOR N. N. R.

In 1940 the Abbott Laboratories presented Abbott's Thiamin Elixir (B_1 Elixir) as a further dosage form of Thiamine Hydrochloride-Abbott. The preparation was found to contain 6.66 mg. of Thiamine Hydrochloride, U. S. P. (2,000 U. S. P. [international] units of vitamin B_1) per fluidounce, in a port wine base containing alcohol 10 per cent and benzoic acid 0.1 per cent as a preservative. In 1941 the Smith-Dorsey Company presented Elixir Thiamin Chloride as a dosage form of thiamin chloride. The elixir is said to be prepared by dissolving thiamine hydrochloride in sherry wine containing 17 per cent alcohol with added sugar. The thiamine content is reported as 6.66 mg. per fluidounce.

It appears to the Council that preparations of this character are undoubtedly intended for repeated and prolonged administration. They will likewise be administered as a tonic to children. The Council feels that it is hardly in the interest of rational therapeutics to make it necessary to take appreciable amounts of alcohol in order to obtain a small amount of thiamine hydrochloride. In addition to this there is no good pharmacologic reason for the incorporation of thiamine hydrochloride in an alcohol solution, and therefore such preparations constitute an unscientific mixture of two therapeutic agents. Physicians who may wish to prescribe alcohol have ready access to this drug in various forms, including preparations listed in the U. S. Pharmacopeia and the National Formulary. The Council felt that the use of a preparation of thiamine hydrochloride in an alcoholic menstruum lends itself to abuse through over the counter sales.

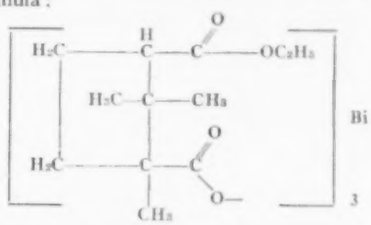
The Council declared Abbott's Thiamin Elixir (B_1 Elixir) and Smith-Dorsey's Elixir Thiamin Chloride unacceptable for inclusion in New and Nonofficial Remedies because under conditions of sale and use such alcoholic solutions are undesirable, and furthermore because they represent an unscientific mixture of two therapeutic agents.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

AUSTIN E. SMITH, M.D., Acting Secretary.

BISMUTH ETHYLCAMPHORATE.—The bismuth III salt of *d*-camphoric acid mono-ethyl ester. It possesses the following formula:



$[C_{12}H_{19}O_4]_3Bi$.—M. W. 890.8. It may be prepared by the interaction of sodium ethylcamphorate and bismuth nitrate in dilute aqueous glycerin solution. The product may then be extracted with chloroform and recovered by the removal of that solvent.

Actions and Uses.—Bismuth Ethylcamphorate is proposed as a means of obtaining the systemic effects of bismuth in the treatment of syphilis. It is a liposoluble compound not so readily absorbed as the water soluble preparation and yet more rapidly absorbed than the suspensions of insoluble bismuth salts in oil. Injection intramuscularly of this preparation produces relatively little local reaction.

Dosage.—For the average adult, 2 cc. (80 mg. of metallic bismuth), administered once a week for a series of ten to fifteen injections.

Tests and Standards.—

Bismuth ethylcamphorate occurs as a white amorphous solid, possessing a faint aromatic odor. It is insoluble in water but soluble in chloroform, ether, ethylene dichloride and vegetable oils. Its solubility in the latter is increased by the addition of camphor. Bismuth ethylcamphorate softens at about 55 C. and melts indefinitely between 61 and 67 C.

Dissolve about 0.25 Gm. of bismuth ethylcamphorate in 25 cc. of ether in a separator; add diluted sulfuric acid sufficient to redissolve the white precipitate which forms at first; shake the mixture and then separate and wash the ether layer once with water: the aqueous acid layer responds to tests for bismuth; extract the ether layer twice with 25 cc. portions of sodium hydroxide solution, evaporate the combined alkaline extracts in a beaker to a volume of about 15 cc., cover the beaker with a watch glass and continue to heat for about two hours; filter, cool and acidify the solution with diluted sulfuric acid and allow the precipitate to crystallize. Separate and recrystallize the product from a small amount of hot water. The melting point of the dried *d*-camphoric acid obtained is from 186 to 188 C.

Place 0.25 Gm. of bismuth ethylcamphorate, accurately weighed, in a tared, wide dish; heat at 75-80 C. under pressure of 10 to 15 mm. of mercury to constant weight: the loss in weight is not more than 2.5 per cent.

Transfer about 0.5 Gm. of bismuth ethylcamphorate, accurately weighed, to a 500 cc. Kjeldahl flask, add 15 cc. of sulfuric acid and 15 cc. of nitric acid and boil gently until the mixture is colorless, adding more nitric acid if necessary. Continue to boil until the excess nitric acid is removed; cool and transfer the acid solution to a beaker, rinsing the flask with several 15 cc. portions of water. Dilute to about 100 cc., add two drops of methyl red solution and add ammonia water dropwise until the solution turns yellow. Add 2 cc. of nitric acid and dilute to about 150 cc. Heat to boiling, add five drops of 10 per cent ammonium phosphate solution and stir vigorously. Then add 40 cc. of the phosphate solution and digest the precipitate on a steam bath for thirty minutes, filter through a tared Gooch crucible and wash the precipitate with 3 per cent ammonium nitrate solution acidified with nitric acid. Dry at 100 C. for thirty minutes and finally ignite to constant weight. The weight of the bismuth phosphate found corresponds to a bismuth content of not less than 21.5 per cent nor more than 23.5 per cent, calculated to the dried substance.

THE UPJOHN COMPANY, KALAMAZOO, MICH.

Bismuth Ethylcamphorate Solution (in oil): Vials 30 cc. Each cubic centimeter of solution contains a suspension of bismuth ethylcamphorate equivalent to 0.04 Gm. of elemental bismuth, camphor 0.10 Gm. and benzyl alcohol 0.025 cc., dissolved in sweet almond oil.

Ampuls Bismuth Ethylcamphorate Solution (in oil): 1 cc. Each cubic centimeter of solution contains a suspension of bismuth ethylcamphorate equivalent to 0.04 Gm. of elemental bismuth, camphor 0.10 Gm. and benzyl alcohol 0.025 cc., dissolved in sweet almond oil.

ASCORBIC ACID-U. S. P. (See New and Nonofficial Remedies, 1941, p. 557).

The following dosage forms have been accepted:

JOHN WYETH & BROTHER, INC., PHILADELPHIA.

Tablets Ascorbic Acid: 10 mg. and 25 mg.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, MARCH 21, 1942

TONSILLECTOMY AND POLIOMYELITIS

The limited occurrence of the paralytic form of poliomyelitis, when contrasted with the widespread dissemination of the virus, suggests that certain factors may exist which determine whether clinical or subclinical disease will result following infection. The occurrence of the bulbar type of the disease after tonsillectomy is an instance of such an additional factor. According to Aycock this involves autarcesis of the host rather than immunity to the virus. The relationship between tonsillectomy and acute anterior poliomyelitis was reported by Sheppard in 1910 and by Ayer in 1928, and it has been reported in more extensive recent observations by Aycock and Luther, Silverman, Stillerman and Fischer, Top and Vaughan and others. Stillerman and Fischer [1] found that tonsillectomy and adenoidectomy had been performed on 10 of 686 patients in a New York epidemic during the month antedating their illness; 6 of the 10 had the bulbar form of the disease. Fischer, Stillerman and Marks [2] found in their study of the Toronto epidemic of 1937 that acute poliomyelitis developed more often among children between the ages of 3 and 12 years in those recently tonsillectomized than in others. The increased incidence was due entirely to the excess of cases of the bulbar form. Among the children with poliomyelitis the incidence of the bulbar form was twice as great in those whose tonsils had been removed at any time previously as in those with tonsils intact. Analysis of the Detroit epidemic of 1939 by Top and Vaughan [3] revealed that for all forms of poliomyelitis the percentage with a history of tonsillectomy at some previous time is higher among patients with poliomyelitis than among the controls in the same areas. Furthermore, whereas bulbar paralysis developed among 4.2 per cent of nontonsillectomized patients, its incidence among patients previously tonsillectomized was 27 per cent.

Aycock,[4] after analyzing the available data, points out that the less common bulbar form predominated in the combined statistics over the spinal form in a ratio of about 5:1 in the cases occurring within thirty days following tonsillectomy. In the thirty to sixty day period after tonsillectomy spinal cases were in the ascendency in the same proportion as they exceed bulbar paralysis in general. The incubation period of poliomyelitis in man is represented by a specific interval of from seven to fourteen days. The concentration of bulbar cases following tonsillectomy in the thirty day group at the specific interval of seven to twenty-one days, as compared with the random distribution of bulbar cases in the thirty to sixty day group and the spinal cases throughout the whole period, constitutes, Aycock believes, a strong indication that the occurrence of the bulbar cases in the thirty day group is specifically related to the operative procedure. In all age groups the percentage of cases which are bulbar was significantly higher in tonsillectomized than in nontonsillectomized persons. Nonparalytic poliomyelitis occurred in the two groups with the same frequency as the bulbar and spinal forms combined. These data suggest that removal of the tonsils is not a determinant between nonparalytic and paralytic poliomyelitis but rather between the bulbar and spinal forms of the paralytic disease.

The high proportion of cases of the bulbar form of poliomyelitis which occur shortly after tonsillectomy is paralleled by Sabin's [5] experiments on monkeys. Sabin observed that mere transitory contact between the normal or injured pharynx or tonsils of monkeys and the virus of poliomyelitis is not enough to produce the disease. However, injection of moderate amounts of virus into the tonsillopharyngeal region produced poliomyelitis in 16 out of 20 monkeys; 13 of these developed the bulbar type of the disease. Of 12 monkeys inoculated intracutaneously or subcutaneously (abdomen) with the same amount of virus, none contracted the disease. These tests show how much more susceptible is the tonsillopharyngeal region. Sabin concluded that the virus progressed along the local peripheral nerves to reach the nuclei of the cranial nerves. The selectivity observed in the occurrence of bulbar poliomyelitis following tonsilectomy in man and its relatively more frequent occurrence in

1. Stillerman, Maxwell, and Fischer, A. E.: Acute Bulbar Poliomyelitis Following Recent Tonsillectomy and Adenoidectomy, Am. J. Dis. Child. **56**: 778 (Oct.) 1938.

2. Fischer, A. E.; Stillerman, Maxwell, and Marks, H. H.: Relation of Tonsillectomy and of Adenoidectomy to the Incidence of Poliomyelitis, Am. J. Dis. Child. **61**: 305 (Feb.) 1941.

3. Top, F. H., and Vaughan, H. F.: Epidemiology of Poliomyelitis in Detroit in 1939, Am. J. Pub. Health **31**: 777 (Aug.) 1941.

4. Aycock, W. L.: Tonsillectomy and Poliomyelitis, Medicine **21**: 65 (Feb.) 1942.

5. Sabin, A. B.: Experimental Poliomyelitis by the Tonsillopharyngeal Route, J. A. M. A. **111**: 605 (Aug. 13) 1938.

tonsillectomized persons suggests that the nasal pharyngeal mucosa is particularly vulnerable and may contain some additional factor which determines the outcome of exposure to the virus. Since tonsillectomy is practically always selective as to time, it would appear desirable to have it performed during the season which does not coincide with the prevalence of poliomyelitis. This measure would probably eliminate a number of cases of the grave and highly fatal bulbar form of the disease.

THE SANITATION OF EATING UTENSILS

An immense increase in travel by rail, ship, plane and motor car and the urbanization of the population have induced millions of people to eat often away from home. The sanitary control of public eating and drinking establishments is an important public health problem.

In fifty-five eating places in Providence, R. I., the methods of dishwashing and the presence on eating utensils of various organisms were investigated.[1] Controlled laboratory experiments were used to determine the requirements for chemical sterilization of glasses with chlorine compounds. An effort was made to educate the managers and employees in the essentials of sanitation and personal hygiene. The investigators visited each establishment twice. They frequently found unclean walls, ceilings and floors, flies in excessive numbers and toilets in poor repair.

The most important single cause of insanitary practices was the abysmal ignorance of managers and employees of accepted sanitary requirements and procedures. The so-called health card required of all employees in these public eating places had degenerated into a mere formality and was without practical significance. The period of exposing eating utensils to hot water or chemical disinfectants was extremely variable and in most instances far too short to insure effective disinfection. The total bacteriologic count was considered a satisfactory index of the sanitary efficiency of methods employed in washing eating utensils. There was no correlation, however, between the high total counts and the presence of specific pathogenic organisms. Hemolytic streptococci, staphylococci and acid-fast bacteria, although they were not identified as Mycobacterium tuberculosis, were readily recovered from eating and drinking utensils. Escherichia coli and Aerobacter aerogenes also were found on some eating utensils. Staphylococcus albus was the most frequent contaminant found. The diphtheria bacillus was not readily isolated nor were any of the organisms associated with Vincent's angina.

The use of chlorine compounds for the disinfection of beverage glasses can be an effective method providing relatively sterile glasses. However, most of the establishments using chlorine disinfection were guilty of gross misuse of this procedure. A concentration of fifty parts per million of available chlorine acting for fifteen seconds was sufficient to cause a reduction of 99.9 per cent in the bacterial counts of beverage glasses artificially contaminated with Staphylococcus aureus and A. aerogenes when the glasses were freed from organic matter before being immersed in the chlorine solution at a temperature of 59 F. Proof of the relationship between methods of dishwashing and the spread of disease in the community is difficult; nevertheless, any physician who visits eating places during rush periods will occasionally detect obvious evidence of the seriousness of this sanitary defect in public eating and drinking establishments. In these times, attention of managers should be called promptly to such glaring opportunities for dissemination of infection.

1. Horwood, Murray P., and Pesare, P. J.: The Sanitation and Bacteriology of Public Eating Utensils, Pub. Health Rep. **57**: 33 (Jan. 9) 1942.

ZINC PEROXIDE AND SULFONAMIDES IN THE TREATMENT OF GAS GANGRENE

The inability of anaerobic organisms to multiply in an environment rich in oxygen has been abundantly demonstrated in experiments in vitro. The spores of these organisms, while more resistant than the vegetable forms, likewise succumb to oxygen even though they require somewhat higher concentrations. Meleney has demonstrated that this holds true for microaerophilic bacteria. These organisms are capable, after initial cultivation on anaerobic plates, to adapt themselves to the air and to grow aerobically. Therefore, in the treatment of infections produced by anaerobic or microaerophilic organisms an agent capable of liberating oxygen slowly and continuously over a long period is desirable. The experiments of Meleney and his associates both in vitro[1] and in vivo[2] demonstrate the effectiveness of zinc peroxide in the treatment of infections caused by these organisms. To be successful, however, the treatment must adhere to the following three principles:

1. The preparation must be active; that is, it must be capable of liberating oxygen when suspended in water or in contact with body fluids. A uniformly active product is now available and has been accepted by the Council on Pharmacy and Chemistry for admission to New and Nonofficial Remedies. It may be used as it comes from the distributors without being sterilized, or it may be sterilized in a dry oven at 140 C. for four hours.

2. The watery suspension (40 per cent) must be applied so that it comes in contact with every part of

1. Johnson, B. C., and Meleney, F. L.: The Antiseptic and Detoxifying Action of Zinc Peroxide on Certain Surgical Aerobic, Anaerobic and Microaerophilic Bacteria, Ann. Surg. **109**: 881 (June) 1939.
2. Meleney, F. L.: Zinc Peroxide in the Treatment of Microaerophilic and Anaerobic Infections, Ann. Surg. **101**: 997 (April) 1935.

the invaded surface, which means that in most instances it must be preceded by a wide exposure and débridement.

3. The dressing must be kept wet so that oxygen may be liberated. Meleney states that with zinc peroxide there is immediate disappearance of odor from the wound and subsidence of all signs of inflammation.

Reed and Orr [3] have shown in guinea pigs that the introduction of zinc peroxide into wounds inoculated with ten times the lethal dose of Clostridium welchi, Clostridium septicum, Clostridium novyi or Clostridium sordelli resulted in a high percentage of recoveries and in a prolongation of the survival time in cases of fatal infection. Almost similar results were obtained by the same authors [4] in guinea pigs from the use of various sulfonamide derivatives placed in the depth of the wound injected with ten times the lethal dose of Cl. welchi, Cl. septicum, Cl. novyi or Cl. sordelli. It was found that the concentration of sulfathiazole in the wound remained high for a longer period than was the case with the other derivatives. The relatively stable concentration of sulfathiazole in the infected or potentially infected tissue was probably an important factor in the superiority of sulfathiazole over sulfanilamide or other sulfonamide derivatives. The use of sulfathiazole resulted in 60 per cent recoveries from oral administration and 97 per cent when introduced directly into the infected wound. All untreated animals died of characteristic gas gangrene in an average of twenty-six hours. Even large doses of sulfathiazole, according to these authors, have either no deleterious influence on the normal healing processes of the wound or at most only a transient influence. They regard sulfathiazole as the most suitable drug for the early treatment of gas gangrene or of potential gas gangrene. Hawking [5] found that application of sulfonamide compounds to the wounds at the same time as insertion of the organisms saved a large portion of the animals infected with Cl. welchi or with Cl. septicum but that it had only slight influence on infection with Clostridium oedematiens. Sulfathiazole was the most successful compound to use in all cases. Local application of sulfathiazole to the wound was more successful in preventing infection than systemic administration by intraperitoneal injection. Delay of two hours in applying the treatment greatly reduced its effectiveness.

The value of sulfonamide derivatives in the treatment of aerobic hemolytic streptococcus, pneumococcus and gonococcus infections has been established. Meleney [6] notes that these infections are characterized by a relatively long primary stage of cellulitis in which there is no destruction of tissue. The value of these preparations in types of infection in which there is early destruction of tissue is yet to be demonstrated.

3. Reed, G. B., and Orr, J. H.: Treatment of Experimental Gas Gangrene with Zinc Peroxide, War Med. **2**: 79 (Jan.) 1942.

4. Reed, G. B., and Orr, J. H.: Local Chemotherapy of Experimental Gas Gangrene, War Med. **2**: 59 (Jan.) 1942.

5. Hawking, F.: Prevention of Gas Gangrene Infections in Experimental Wounds by Local Application of Sulfonamide Compounds and by Sera, Brit. M. J. **1**: 263 (Feb. 22) 1942.

6. Meleney, F. L.: The Important Anaerobic Infections and the Use of Zinc Peroxide in Their Control, U. S. Nav. M. Bull. **40**: 53 (Jan.) 1942.

Current Comment

EXPERIMENTAL PROCARCINOGENIC EFFECT OF BIOTIN

Attention is drawn once again to biotin and its relation to experimental cancer. The high biotin content of tumor tissue has been discussed recently in these columns.[1] Now the striking report is made [2] that biotin concentrates and crystalline biotin have a definite procarcinogenic action in rats. The oral administration of the dyestuff butter yellow to experimental animals maintained on a suitable basal diet results in the development of hepatic tumors in a high proportion of cases. Butter yellow incidentally is a dyestuff that is not used to color butter or other foods. The dietary conditions can be so chosen that with butter yellow a 96 per cent incidence of live tumors occurs in one hundred and fifty days. In studies designed to determine the effectiveness of various dietary factors in protecting rats against butter yellow it was observed [3] that the addition of riboflavin and of casein to the basal diet gave much protection. The tumor incidence at the end of one hundred and fifty days had decreased from 96 per cent to 7 per cent. This effect, though striking, was not as complete as that obtained by supplements of dried liver or yeast. Accordingly, the influence of the addition of other members of the B complex vitamins was studied. The addition of biotin concentrates or of crystalline biotin to a diet rendered protective against butter yellow feeding by the addition of riboflavin and casein supplements did not result in greater protection but, on the contrary, gave less protection to the animals. In three sets of experiments in which rats were maintained on diets affording a high degree of protection, biotin supplements were found to "break through" the protection. Whereas in the control animals ingesting the protective diet only 1 rat out of 28 developed a liver tumor, the addition of biotin to the same diet in another group of animals resulted in liver tumors in 22 out of a total of 50 animals. These striking results suggest a number of speculative conclusions which may profitably be discussed only when further experimental data are available. The procarcinogenic action of biotin in these studies seems clear. The possibility of producing an opposite effect by a biotin deficiency is of considerable interest. The announcement at this time [4] of the crystallization of the biotin inactivating protein avidin is most propitious for this line of future investigation.

1. Biotin in Tumor Tissue, Current Comment, J. A. M. A. **117**: 622 (Aug. 23) 1941.

2. du Vigneaud, Vincent; Spangler, J. M.; Burke, Dean; Kensler, C. J.; Sugiura, Kanematsu, and Rhoads, C. P.: Science **95**: 174 (Feb. 13) 1942.

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MEDICINE AND THE WAR

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medicine and the war, and such other information and announcements as will be useful to the medical profession.

MEDICAL RESERVE OFFICERS HOLDING KEY CIVILIAN POSITIONS

The following memorandum was sent by the Adjutant General's Office on March 2 to all corps area commanders and to the Surgeon General:

1. Medical Reserve officers who occupy key civilian positions fall into two general categories, viz. (*a*) those in the federal employ and (*b*) those not in the federal employ.

2. War Department instructions have been published which govern the deferment of reserve officers in federal employ. Under those instructions no reserve officers so employed will be granted deferment beyond March 31, 1942. Those desiring to continue beyond that date in civilian pursuits must tender their resignations from the Officers' Reserve Corps. Reserve officers at present in the War Department Reserve Pool who are federal employees and whose resignations are not accepted prior to April 1, 1942 will be relieved from the War Department Reserve Pool by individual letters from this office.

3. A similar plan will govern the deferment of reserve officers not in federal employ who are engaged in civilian capacity in the medical profession:

(*a*) Except for those who have not completed one year's internship, no such reserve officer will be granted deferment beyond March 31, 1942. After that date all such officers will be considered available for active duty whenever their services are required.

(*b*) When it is essential in the interest of the national health or safety that a reserve officer engaged in civilian status in the medical profession should continue in that civilian status, he may tender his resignation from the Officers' Reserve Corps.

(1) Each such tender should be addressed to the Adjutant General, Washington, D. C., attention Reserve Division, and will be accompanied by supporting data establishing the necessity for such resignation.

(2) These supporting data will include a written statement from the appropriate county or state public health official that the continuation of the individual in his civilian occupation beyond March 31, 1942 is considered essential to the public welfare of the county or other appropriate governmental subdivision concerned.

TEMPORARY HOSPITALIZATION FOR CIVILIANS INJURED AS RESULT OF ENEMY ACTION

Temporary hospitalization for civilians injured as the result of enemy action is provided in an agreement announced jointly on March 13 by Administrator Paul V. McNutt of the Federal Security Agency and Director James M. Landis of the Office of Civilian Defense. Financed by special funds allotted to the U. S. Public Health Service by the Federal Security Administrator from funds made available to him by President Roosevelt from his emergency fund, the agreement provides that:

1. In the event of injury to civilians from air raids or other enemy action, all voluntary and governmental hospitals of the nation may serve as casualty receiving hospitals of the Emergency Medical Service. Hospitals will be reimbursed by the federal government for the care of such casualties at established rates.

2. Certain hospitals and other appropriate institutions in "safe areas" are to be designated as emergency base hospitals for reception of casualties or other patients whom it may be necessary to evacuate from casualty receiving hospitals. Those hospitals will also be reimbursed by the federal government at established rates for hospital and medical care. In addition, federally owned medical equipment may be lent to such hospitals, and their medical staffs will be supplemented by physicians of the area, who will be commissioned in the reserve corps of the U. S. Public Health Service.

3. This emergency hospital program will be carried out by the Medical Division of the Office of Civilian Defense in cooperation with the U. S. Public Health Service and the state and local authorities. It was also announced that special sections have been organized in the Medical Division of the Office of Civilian Defense and in the U. S. Public Health Service to carry out the joint program.

Dr. George Baehr, chief medical officer of the Office of Civilian Defense, said that the line of evacuation of hospital populations from cities to the base is to be determined in collaboration with the military and the state evacuation authorities as well as with regional, state and local defense councils.

Dr. Baehr emphasized that the management and control of local casualty receiving hospitals, as well as of emergency base hospitals, will remain the responsibility of the local or state authorities, but all hospitals which admit civilians disabled by enemy action, including sabotage, would be reimbursed. Except for assignment of medical staff and loan of equipment to base hospitals, additional costs will not be a federal responsibility unless authorized in advance, he said.

In establishing emergency base hospitals, emphasis will be placed on the relative safety of the area and the availability of existing hospitals and other suitable institutions to which civilian casualties and other hospital patients could be promptly transferred from urban hospitals in the target areas. Hospitals will be classified on the basis of size, equipment and standards of operation. Surveys of hospital facilities have been under way for some time.

It is proposed to begin immediately the organization of the necessary medical staffs for the base hospitals and to provide for their prompt availability when needed by commissioning them in the reserve corps of the U. S. Public Health Service. These physicians, surgeons, specialists and dentists will receive rank, pay and allowances equivalent to those of the medical corps of the Army. The commissioned officers will be selected from older age groups and from those with physical disabilities which make them ineligible for military service. Women physicians will also be eligible.

The physicians will be selected by regions so that, as far as possible, they may be assigned to service in the regions of the country in which they live. Because they are to function as balanced professional staffs, they will be recruited largely as affiliated hospital units from the staff of civilian hospitals and cleared through the new Procurement and Assignment Service for Physicians, Dentists and Veterinarians.

The following is the text of the agreement between the Federal Security Agency and the Office of Civilian Defense:

AGREEMENT BETWEEN THE FEDERAL SECURITY AGENCY AND THE OFFICE OF CIVILIAN DEFENSE

Subject: Temporary Hospitalization and Medical Care Necessitated by Enemy Action to Civilians.

In an order dated Feb. 6, 1942 the President of the United States allocated funds to the Federal Security Administrator for the following stated purposes:

> "to be expended by the administrator of the Federal Security Agency, or through such federal or other agencies as he may designate, for providing temporary aid necessitated by enemy action to civilians, other than enemy aliens, residing in the United States: (1) who are disabled;

(2) who are dependents of civilians who are killed, disabled, interned or reported as missing, or (3) who are otherwise in need of assistance or services. This allocation is not intended to cover civil or other personnel of the federal government for whom other provisions are contemplated."

In order to carry out that part of the order which relates to medical and hospital care, Federal Security Administrator Paul V. McNutt and Office of Civilian Defense Director James M. Landis have agreed that the Federal Security Agency, through the United States Public Health Service, will carry out the following program:

Casualty Hospitals.—All the hospitals in the nation, voluntary and governmental, may serve as casualty hospitals of the Emergency Medical Services established by the Office of Civilian Defense for the care of civilian casualties caused by enemy action. The management and control of such hospitals will not be affected by this plan. Cash payments will be given to such hospitals caring for casualties pursuant to the President's order, at a per diem rate of $3.75.[1] Any additional costs will not be a federal responsibility unless specifically authorized in advance to meet exceptional circumstances.

Emergency Base Hospitals.—These hospitals will include existing, new or improvised facilities desirably located in "safe areas" outside heavily populated centers and will be used for the care and treatment of civilian casualties and other patients evacuated from urban hospitals because of enemy action.

The Medical Division of the Office of Civilian Defense, in cooperation with the U. S. Public Health Service and state and local medical directors of the Emergency Medical Services, will press for a prompt conclusion existing surveys of such emergency hospital needs and will make recommendation for meeting such needs. Emphasis will continue to be placed on the vulnerability of the area, availability of existing federal, state and local hospital facilities, and other institutions suitable for conversion into emergency base hospitals and the location, number, size and equipment of such hospitals, in order to develop a list to be approved by the Medical Division of the Office of Civilian Defense. The administration of such emergency base hospitals will continue to be a responsibility of state and local authorities. For hospitals which are approved as regards location and otherwise by the Medical Division of the Office of Civilian Defense, federal assistance will be available as follows:

1. A limited amount of hospital equipment will be lent for use in approved emergency base hospitals by the Medical Division of the Office of Civilian Defense. The equipment will remain federal property and will be subject to transfer to other localities or states in accordance with national emergency needs.

2. The medical staff of such hospitals will be supplemented as necessary by physicians including specialists commissioned in the reserve of the United States Public Health Service and assigned, on request, by the Surgeon General thereof.

3. Reimbursement will be made on a per diem basis for temporary care of civilian casualties as above provided for casualty hospitals.

In consideration of the per diem allotment for the care of these patients, it is expected that the hospitals will provide the nursing, technical and subordinate staff and other operating expenses.

Joint effort will be made to obtain assistance under the Community Facilities Act, approved by the President on June 28, 1941, for projects coming within the purview of that act, and of other federal legislation, to supplement existing hospital facilities for the care and treatment of casualties.

Medical Personnel.—Emergency base hospitals for the care of evacuated casualties conceivably may require a large staff of physicians, surgeons and other specialists, including dentists, some of whom must be of high professional caliber. Since such a balanced technical staff cannot be assembled hurriedly in time of need and must be enrolled for future service, as are affiliated general hospital units of the Army, it is proposed to expand the commissioned reserve of the United States Public Health Service for this purpose.

Recruiting will be carried on in collaboration with the Procurement and Assignment Service in accordance with existing agreements. In order not to interfere with the supply of physicians for the Army and Navy, recruitment will be largely from the older age groups, from physicians with minor physical disabilities which make them ineligible for military service, and from women physicians. Some specialists may be given a consultant status, so as to be available for part time duty.

Other members of the reserve, especially obstetricians, pediatricians, dentists and women physicians, also will be appointed for service in reception areas into which women and children are evacuated.

Nursing and Other Services.—The United States Public Health Service and the Medical Division of the Office of Civilian Defense will cooperate with the American Red Cross, responsible state and local officials, and other organizations in arranging for nursing, technical and other services in emergency base hospitals. The cost of such services will not be federal responsibility.

Field Casualty Service.—In accordance with instructions contained in Medical Division Bulletins 1 and 2 of the Office of Civilian Defense, the responsibility for providing local field casualty services, including the organization of emergency field units, the establishment of casualty and first aid posts, and arrangements for casualty transportation, will continue to be a responsibility of state and local authorities.

Approved: PAUL V. MCNUTT. March 2, 1942.

Approved: J. M. LANDIS. Feb. 26, 1942.

1. This is the rate of reimbursement established by the Federal Board of Hospitalization for federal beneficiaries in government hospitals and may be changed as conditions require.

APPOINTMENTS BY OFFICE OF CIVILIAN DEFENSE

Dr. John S. Coulter, associate professor of physical therapy, Northwestern University Medical School, Chicago, has been appointed regional medical officer of the sixth Civilian Defense region with headquarters in Chicago. Dr. Coulter was a member of the regular army corps for about ten years and during the first world war commanded a hospital center in Savenay, France. Since his resignation from the Army Medical Corps in 1920 he has practiced medicine in Chicago. He is a member of the Council on Physical Therapy of the American Medical Association and is the author of a book entitled "History of Physical Therapy."

Dr. Dudley A. Reekie, chief medical officer of the Tennessee Valley Authority, Chattanooga, Tenn., has been appointed regional medical officer of the first Civilian Defense region with headquarters in Boston, to succeed Dr. Allan M. Butler of Boston, who resigned to become head of the department of pediatrics at Massachusetts General Hospital. Dr. Reekie, a native of New Zealand who came to the United States in 1920, is a diplomate of the National Board of Medical Examiners. He served several years with the Kentucky State Board of Health as field director of county health work. During the first world war he served as a radio operator with the Royal Naval Volunteer Reserves.

Dr. Leonard A. Scheele, passed assistant surgeon, U. S. Public Health Service, has been assigned to the Washington staff of the medical division of the Office of Civilian Defense. Dr. Scheele graduated in medicine in 1933 at Wayne University College of Medicine, Detroit, and was commissioned to the Public Health Service following completion of his internship. After special training in clinical cancer work at Memorial Hospital for the Treatment of Cancer and Allied Diseases in New York he was assigned to the National Cancer Institute, Bethesda, Md., as consultant on cancer control.

Dr. Harold Marks, passed assistant surgeon (reserve), U. S. Public Health Service, joined the medical division of the Office of Civilian Defense recently. Dr. Marks graduated from the University of Illinois College of Medicine, Chicago, in 1936, interned at Sacred Heart Hospital, Spokane, Wash., and practiced in the state of Washington until 1940, when he entered the University of Chicago for a course in hospital administration. Before being assigned to the Office of Civilian Defense he was stationed at the National Institute of Health and was engaged in making medical surveys of medical care in defense communities.

Mr. Gerald E. Arnold, chief water purification engineer for the water department of San Francisco, has been appointed regional sanitary engineer for the ninth Civilian Defense region,

which includes California, Idaho, Montana, Nevada, Orgeon, Utah and Washington. Mr. Arnold was commissioned sanitary engineer (reserve) in the U. S. Public Health Service.

Mr. William H. Carey Jr. has been appointed regional sanitary engineer for the sixth and seventh Civilian Defense regions, plus Indiana and Kentucky, with headquarters in Chicago. Mr. Carey is a graduate of the University of Michigan College of Engineering and was formerly junior engineer with the Chicago Sanitary District and analyst and public health engineer with the U. S. Public Health Service and assistant engineer with the Michigan State Department of Health.

CARE OF BABIES DURING AIR RAIDS

Instructions as to the special care of babies in the event of an air raid, based in part on the experience of British cities, have been prepared by the American Committee on Maternal Welfare, 650 Rush Street, Chicago.

The committee is composed of the leading medical, public health, nursing and hospital organizations of the country. Aside from the immediate need of shelter from bomb explosions, the most important fact to keep in mind, the British have learned, is that the mother's mental attitude is baby's best guaranty against air raids. "However frightened you may feel," the committee quoted from instructions issued by the British National Baby Welfare Council, "keep outwardly calm, so that the child's confidence in your own protectiveness may not be shaken.

"Never speak of the raid in the child's hearing if you can avoid it. Mental impressions are formed much earlier than most people realize. Many of the problem cases among grown-ups of the present day owe their condition to their parents having talked continually in the presence of the children about past and future air raids, about their own terror, and the effect of this on the child."

When the raid signal sounds, the first move should be in the direction of the nearest shelter. If there is no shelter, take the baby to the safest room in the house or to a closet under the stairs or under a table or bed, so that he may be protected from flying débris, which presents the most frequent danger. Take with him garments enough to keep him warm according to the season, a basket or pillow on which he can lie, a first aid outfit in case of need; a toy to amuse him; his bottle of milk and bottle of water, together with extra diapers and related equipment. The baby's ears should be blocked with cotton to minimize the effects of concussion, leaving plenty outside so that it may be easily withdrawn afterward. If the raid should come while the baby is away from either house or shelter—for an airing in the park, for instance—find the nearest wall or ditch, however low, place the baby on the ground beside it, with pillows from the baby carriage or a heavy coat under and over him, and lie down beside him.

The problems of baby and mother in wartime and their safety will be discussed at the second annual Congress on Obstetrics and Gynecology, sponsored by the committee, in St. Louis, April 6 to 10.

THE COLLECTION OF MEDICAL MUSEUM MATERIAL

Col. J. E. Ash, M. C., U. S. Army, curator of the Army Medical Museum, Washington, D. C., states that the so-called museum and medical art activity of the army is being organized as a subdivision of the Museum Division of the Surgeon General's Office. The purpose is to obtain trained personnel, including clinical photographers and medical artists, who will serve with the expeditionary forces and in the larger army hospitals in order to collect pathologic material, pictorial records of diseases and injuries and their treatment, weapons, missiles and protective devices and arrange for their shipment to the Army Medical Museum. It is proposed also to collect similar material that might come to the attention of civilian pathologists and to add it to the collections of the armed forces. The civilian material in this category will include that arising from airplane crashes, civilian bombing, fires, specific epidemics, particularly the virus diseases, encephalitis, influenza, poliomyelitis and atypical pneumonia. All cases sent to the museum should be accompanied by complete clinical data and necropsy protocols. Facilities are available, on request, to cover the shipment of this material and to process photographic material, including copying. Contributors would be credited in the museum files and would not lose control of their material. Colonel Ash welcomes suggestions that will aid in making this activity a success.

ARMY NEEDS TEN THOUSAND NURSES

The U. S. Army Nurse Corps has immediate need for three thousand qualified registered nurses, and for ten thousand in all before the end of 1942, to keep pace with the expanding army, the War Department announced on March 13. Applicants who can fulfil the Army Nurse Corps requirements will be appointed in the grade of Nurse, with the relative rank of Second Lieutenant. The pay is $840 a year in addition to maintenance and uniform equipment. Appointments as nurse will be for the duration of the war. Promotions to higher grades are made in peace time only after three years of service, but this rule no longer applies. The appointment authority for the Army Nurse Corps is vested in the commanding generals of the various corps areas. However, applications for appointment may be made through any local office of the National Red Cross Nursing Service, which is acting as procurement agency for the corps. When the quota for any particular corps area may have been filled, applications will be referred to another corps area where a shortage exists.

An eligible applicant must be of good character, unmarried, a citizen of the United States, between 22 and 30 years of age, at least 5 feet tall and of standard weight for her age and height. She must be a graduate of an accredited high school giving a four year academic course and of a school of nursing of approved standards, and a registered nurse. Application papers must be accompanied by an unmounted autographed photograph of the applicant taken within the preceding two years, and a statement from the proper official of the high school from which she was graduated, giving the date of graduation and her numerical place in the class.

The physical fitness of an applicant is determined by an examination by a board of medical officers at the nearest army post.

ONE DAY "WAR SESSIONS"

The American College of Surgeons will hold one day "War Sessions" between April 1 and May 1 on problems of military service and civilian defense for medical and hospital personnel, as follows:

Date	Place	States	Headquarters
April 1	Portland, Me.	Maine, Vermont, New Hampshire	Eastland Hotel
April 3	Albany, N. Y.	New York	DeWitt Clinton Hotel
April 7	Denver	Colorado, Wyoming	Cosmopolitan Hotel
April 10	Salt Lake City	Utah, Idaho	Hotel Newhouse
April 13	Portland, Ore.	Oregon, Washington, Montana	Multnomah Hotel
April 16	San Francisco	Northern California, Nevada	Fairmont Hotel
April 18	Los Angeles	Southern California	Biltmore Hotel
April 21	Phoenix, Ariz.	Arizona, New Mexico	Westward Ho Hotel
April 24	Dallas, Texas	Texas, Oklahoma	Baker Hotel
April 28	Madison, Wis	Wisconsin	Loraine Hotel
May 1	Minneapolis	Minnesota, South Dakota, North Dakota	Nicollet Hotel

During March similar meetings were held in Louisville, Ky.; Nashville, Tenn.; St. Louis; Chicago; Detroit; Columbus, Ohio; New Orleans; Atlanta, Ga.; Jacksonville, Fla.; Durham, N. C.; Baltimore; Harrisburg, Pa.; Newark, N. J., and New Haven, Conn.

The meetings open at 9 a. m. with panel discussions on treatment of war injuries for the medical profession and a forum on civilian defense as related to hospitals, led by a medical officer of the United States Office of Civilian Defense, for hospital personnel. A joint meeting also is held with medical officers of the Army, the Navy and the Office of Civilian Defense, as speakers. At the luncheon the Procurement and Assignment Service in relation to the medical profession and to hospitals is discussed by Major Sam F. Seeley, Executive Officer, a specially appointed delegate. In the afternoon panel discussions for the medical profession are held on treatment of wounds of soft parts and on fractures, and for hospital representatives on special problems incident to the war as affecting hospitals.

The success of the March meetings justified their extension to the remaining states, as shown by the April schedule. Hospital associations and state and county medical societies are cooperating with the American College of Surgeons in conducing the sessions.

THE WORK OF NURSES IN CIVILIAN DEFENSE

A nursing consultant is on duty as a member of the staff of the Medical Division of the Office of Civilian Defense in Washington, and the Subcommittee on Nursing of the Health and Medical Committee of the Office of Defense Health and Welfare Services also serves as the Nursing Advisory Committee of the OCD. To assist the regional offices of civilian defense, field nursing consultants of the U. S. Public Health Service, the U. S. Children's Bureau and the American Red Cross have been made available for consultation. One nurse representing the Red Cross and another representing one of the other two agencies have been assigned to each state. The most recent development in the nursing program is the establishment of state nursing councils, which are made up of representatives of nursing organizations, official agencies with nursing programs and the Red Cross. Nurses are required in the Emergency Medical Service now being developed by the medical division of the OCD for the care of casualties in hospitals and for service with emergency medical field units. Nurses will also be required for service in emergency base hospitals to be established in protected rural areas if needed for the reception of civilian casualties due to enemy action. Both the OCD and the Red Cross are urging promotion of the volunteer nurses' aide program to train assistants for nurses in casualty receiving hospitals and in field casualty services. Nurses are being urged by the medical division to arrange to teach home nursing courses, so that more women will be ready to care for sickness in their own homes during an emergency and relieve the hospitals of some of their load. Nurses are also asked to take Red Cross first aid courses so that they may be prepared to help in casualty services and also to qualify as instructors for first aid courses.

JAPANESE BURN YALE-IN-CHINA HOSPITAL

In a broadcast from Chungking, January 16, published in the February issue of *China at War*, the Voice of China observer spoke as follows concerning Japanese vandalism at the Yale-in-China Hospital after the Japanese began their retreat from Changsha: The finest exposition of the Japanese "new order" was provided by their wanton vandalism at the Yale-in-China Hospital. This magnificent two hundred bed establishment, situated outside of Changsha proper, was occupied by the Japanese between January 3 and 5. When the enemy occupied the hospital, the Chinese staff commanders held a conference to discuss whether or not to shell the building. They decided against it although it was an easy target for their heavy guns. Before they left, however, the Japanese set fire to the buildings, destroying about 80 per cent of them. Fortunately, owing to the foresight of the principal, Dr. Winston Pettus, and with the assistance of soldiers provided by the government, practically all equipment and the staff itself had been safely evacuated several days before the Japanese arrived.

DR. LANZA ON DUTY IN SURGEON GENERAL'S OFFICE

Dr. A. J. Lanza, member of the Council on Industrial Health of the American Medical Association, has been appointed lieutenant colonel in the medical corps of the army and assigned to the Division of Industrial Health in the Office of the Surgeon General, Washington, D. C. Lieutenant Colonel Lanza will be chief of the Occupational and Military Hygiene Subdivision, Preventive Medicine Division, which was formed on April 18, 1941 and which has the responsibility of initiating, coordinating and supervising all activities of the medical department in connection with the industrial hygiene program of the army. This subdivision has been engaged in making surveys of occupational hazards and diseases in army operative plants.

SOLDIERS IN COMBAT AREAS TO CARRY SULFANILAMIDE TABLETS

The War Department announced on March 5 that every American soldier who goes into a theater of operations will be equipped with twelve sulfanilamide tablets in a special spill proof metal box as a standard addition to the first aid equipment of all troops in combat areas. Medical officers attached to units are to instruct the soldier in the proper use of the tablets, and careful checks are to be made periodically to see that each soldier carries the tablets. Experience in this war already has demonstrated the efficacy of the drug under war conditions, the War Department says. The small special container for the tablets can be operated with one hand by sliding the top of the box back, thus releasing a single tablet. Directions for use are printed on the back of the box.

MEDICAL LICENSURE IN RELATION TO THE ACCELERATED MEDICAL COURSE

The Federation of State Medical Boards of the United States has mailed to all state boards of licensure and registration, the District of Columbia, Alaska and Puerto Rico, and to the deans of medical schools, a statutory description of medical schools from which present graduates are eligible for licensure; also a resolution adopted by the federation endorsing the proposed accelerated course of medical education as a war emergency measure and pointing out that it is not expected to extend beyond the present period of the war. The proposal to accelerate the training of medical students so they will be able to graduate after three calendar years of instruction will raise questions concerning medical licensure. The memorandum states that in the following nine states and the territory of Puerto Rico there are statutory provisions that will have to be modified, probably by legislative amendment, before licenses can be granted to persons who have graduated after three calendar years of instruction: Georgia, Illinois, Kansas, Maryland, Michigan, Nebraska, New Jersey, South Carolina and Virginia.

In the following sixteen states and the District of Columbia, statutory provisions obtain that will necessitate rather liberal construction, either by special state board action or by state's attorney general's opinion, to permit the granting of licenses: California, Connecticut, District of Columbia, Indiana, Kentucky, Massachusetts, Minnesota, Mississippi, Missouri, Montana, North Carolina, North Dakota, Oregon, Pennsylvania, Tennessee, Texas and Utah.

In the following eleven states the statutory provisions seem broad enough to permit the granting of licenses to such graduates if the examining boards or other state approving agencies will recognize a medical school that graduates students after the abbreviated course of study: Alabama, Delaware, Florida, Iowa, Louisiana, Maine, New Hampshire, New York, Ohio, South Dakota and Wyoming. In these states, if standards have been set up by examining boards or other approving state agencies by rule or regulation, and if existing standards preclude the licensure of graduates after abbreviated courses, the rules or regulations must be amended to permit such licensure.

In the following five states and the territory of Alaska, graduates after abbreviated courses may obtain licensure if the school of graduation is approved by the Association of American Medical Colleges: Alaska, Arizona, New Mexico, Nevada, Oklahoma and Washington.

In the following seven states licensure may be obtained if the school of graduation is approved by the Council on Medical Education and Hospitals of the American Medical Association: Arkansas, Colorado, Idaho, Rhode Island, Vermont, West Virginia and Wisconsin.

In the material sent out by the Federation of State Medical Boards of the United States, as indicated, there are in addition to the foregoing information expressions of opinion from various state licensing boards and some attorney generals of states with regard to the question of licensure in relation to the accelerated medical course as it pertains to the individual states and territories.

MEDICAL SUPPLIES FOR RUSSIA

Edward C. Carter, president of Russian War Relief, Inc., announced on March 4 that one of the largest shipments of medical supplies and foods contributed by American citizens had been made to Russia. The shipment included fifteen thousand surgical needles, an x-ray machine, thirty cases of assorted pharmaceuticals, including gauze and adhesive plaster, 5 tons of acetophenetidin, 10 tons of saccharin, thirty-seven thousand two hundred cans of condensed milk and two million American cigarets, each package bearing a label in Russian expressing admiration for the fight the Russian people are making. The shipment was assembled and dispatched by Russian War Relief, Inc., 535 Fifth Avenue, New York.

TRAINING MEDICAL OFFICERS

A class was graduated from a special course in the Medical Field Service School, Carlisle Barracks, Pa., February 20. A second special officers' course of four weeks' duration will be given at the Field Service School beginning March 13. The commandant of the Field Service School, Brig. Gen. Addison D. Davis, M. C., U. S. Army, awarded diplomas to the following graduates:

MEDICAL CORPS

Major Clifford A. Best, Manning, Iowa.
1st Lieut. Marion G. Brown, Detroit.
Major John B. Chester, Nashville, Tenn.
Capt. Clarence E. Dungan, Almond, N. Y.
Capt. Arlo K. Cox, Watonga, Okla.
Capt. James K. Goldstene, Chicago.
1st Lieut. Ernst A. Griep, Quincy, Ill.
Major William A. Hadly, Pittsburgh.
Capt. William H. Houston, Palo Alto, Calif.
Capt. Paul D. Keller, Minkcreek, Idaho.
Capt. Raymond A. Lawn, Minneapolis.
Capt. William C. Lindstrom, Oklahoma City.
Capt. John G. McKeon, Albany, N. Y.
1st Lieut. Edward G. McNamara, Chicago.
Major Walter C. Mohr, Chicago.
Capt. Michael R. Murphy, Cadillac, Mich.
Capt. Isaiah R. Salladay, Pierre, S. D.
Capt. George I. Sneidman, Hartford, Conn.
1st Lieut. Sherburn M. Stanley, Asheville, N. C.
1st Lieut. Gustaf Sweet, Providence, R. I.
Major William E. Williams, Austin, Texas.
1st Lieut. Edwin C. Yeary, Elmore City, Okla.

MEDICAL ADMINISTRATIVE CORPS

2d Lieut. John O. Andrews, Ottawa, Ill.
Capt. David M. Goldberg, Peabody, Mass.

TEXTBOOK ON WAR GASES

"Protection Against Gas," a textbook on war gases to be used for instruction of public employees and volunteers enrolled in the various groups of the United States Citizens' Defense Corps, has been issued by the U. S. Office of Civilian Defense. The book was prepared by the War Department under the direction of the Chief of Chemical Warfare Service, U. S. Army, with suggestions of the National Technological Civil Protection Committee, a special advisory committee of engineers. The section on "First Aid Treatment of Gas Casualties" was prepared with the assistance of the Medical Division of the Office of Civilian Defense. The seventy-five page manual contains descriptions of the principal gases, their effects and the first aid measures to be used in the care of persons who have been subjected to gas attack. Methods of individual protection, which include the use of masks and wearing of protective clothing, and methods of collective protection such as use of gas proof shelters and methods of decontamination, are described. There is a chapter on protection of animals, especially horses and homing pigeons.

MINNESOTA HOSPITAL UNIT ON ACTIVE DUTY

The University of Minnesota Medical School, Minneapolis, at the invitation of the Surgeon General of the Army, has provided the staff for the Twenty-Sixth U. S. General Hospital unit, which was recently called to active duty and stationed in the South for a period of training. During World War No. 1 the University of Minnesota Medical School, in cooperation with the Mayo Clinic, provided a staff for Base Hospital No. 26, which served at Allerey, France.

ILLINOIS PLASMA PROCURING PROGRAM

The Illinois Department of Public Health, at the request of Governor Green, is formulating plans for collecting, processing and distributing throughout the state blood plasma to be used in possible civilian disasters without infringing on territory already given over to American Red Cross projects for collecting blood for the armed forces. The department expects to call for volunteer donors for civilian defense and to process the blood in a laboratory approved by the National Institute of Health. The Illinois plan, which has been approved by the Office of Civilian Defense in Washington, will obviate the need for independent local plasma programs in the down state area and will avoid the danger attendant on having local plasma supplies processed in unapproved laboratories. The Illinois Department of Public Health encourages local communities which have the facilities to do so to examine, type and register volunteer blood donors who could be called on for person to person transfusions in case of need. This type of transfusion, the state health department says, could be used for later treatments after the emergency administration of plasma.

COLUMBIA UNIVERSITY HOSPITAL UNIT ORDERED TO ACTIVE SERVICE

The Second U. S. Army General Hospital Unit, consisting of fifty-five members of the staffs of the College of Physicians and Surgeons, the School of Dental and Oral Surgery and the Columbia-Presbyterian Medical Centers, have been called to active duty. The chief of the surgical service is Dr. W. Barclay Parsons, associate professor of clinical surgery, and the chief of the medical service is Dr. Yale Kneeland Jr., assistant professor of medicine, both of whom are lieutenant colonels. Other members of the faculty have been granted leaves of absence to enter active service with the Medical Corps of the Army and Navy.

WOMEN AVAILABLE FOR WAR INDUSTRIES

A report just issued by the United States Department of Labor states that nearly six million women can be recruited for work in war industries during 1942. One third will be drawn from the sixteen million five hundred thousand women now in the 18 to 44 age group who also do their own housework without drawing into the labor market mothers from families with children under 10. The Labor Bureau recommends that women be taken into factories from converted or curtailed consumer goods industries before those with children under 10 are drawn into factory work. It is pointed out that five hundred thousand women were already in the total war labor force in January and that this total is expected to increase by anywhere from five million to fifteen million by 1943.

DR. BAYNE-JONES ON DUTY IN SURGEON GENERAL'S OFFICE

According to the *Army and Navy Journal*, Lieut. Col. Stanhope Bayne-Jones, medical reserve corps, U. S. Army, has reported for duty in the Office of the Surgeon General, Washington, D. C., and assigned as chief of the subdivision of epidemiology. Colonel Bayne-Jones, who in civil life is professor of bacteriology at Yale University, New Haven, Conn., entered the reserve corps in 1915 and served throughout the first world war.

STOVES AND MEDICAL SUPPLIES FOR RUSSIA

In a shipment of relief supplies from an Atlantic port by Russian War Relief, Inc., there were thousands of field type kerosene stoves which had been urgently requested by the Russian authorities for use in hospital tents and refuge colonies, in addition to 12,000 ounces of quinine hydrochloride, 10,000 ounces of quinine sulfate and other medical supplies. This is the sixth shipment of supplies to Russia by Russian War Relief, Inc., 535 Fifth Avenue, New York.

ORGANIZATION SECTION

OFFICIAL NOTES

THE ATLANTIC CITY SESSION

The Annual Golf Tournament

The American Medical Golfing Association will hold its twenty-eighth annual tournament at Seaview Country Club, Atlantic City, on Monday, June 8.

FORTY TROPHIES AND PRIZES

Thirty-six holes of golf will be played in competition for the forty trophies and prizes in the eight events. Trophies will be awarded for the Association Championship, thirty-six holes gross, the Will Walter Trophy; the Association Handicap Championship, thirty-six holes net, the Detroit Trophy; Championship Flight, First Gross, thirty-six holes, the St. Louis Trophy; Championship Flight, First Net, thirty-six holes, the President's Trophy; Eighteen Hole Championship, the Golden State Trophy; Eighteen Hole Handicap Championship, the Ben Thomas Trophy and the Atlantic City Trophy; Maturity Event, limited to Fellows over 60 years of age, the Minneapolis Trophy; and the Oldguard Championship, limited to competition of past presidents, the Wendell Phillips Trophy. Thirty other prizes will be awarded for the various flights.

ATLANTIC CITY GOLF COMMITTEE

The Atlantic City Golf Committee is under the chairmanship of Dr. Walt P. Conaway, 1723 Pacific Avenue, Atlantic City, who managed the 1925 tournament at Seaview, the 1935 competition at Northfield Club and the 1937 tournament at Seaview. Assisting Dr. Conaway on the Atlantic City committee are Drs. John Pennington and Karl M. Scott.

TWO EIGHTEEN HOLE COURSES

The 1942 tournament of the American Medical Golfing Association will be played over the two eighteen hole championship courses of the Seaview Country Club at Absecon, N. J. Following the tournament the Annual Golfers' Banquet will be held at the spacious clubhouse beginning at 7 p. m., after which the prizes will be distributed. The officers of the American Medical Golfing Association anticipate that medical golfers from all parts of the United States will play thirty-six holes of golf at Seaview on June 8.

APPLICATION FOR MEMBERSHIP

All male Fellows of the American Medical Association are eligible and cordially invited to become members of the American Medical Golfing Association. Write Executive Secretary Bill Burns, 2020 Olds Tower, Lansing, Mich., for an application blank. Participants in the American Medical Golfing Association tournament are required to present their home club handicap, signed by the club secretary, at the first tee on the day of play. No handicap over thirty is allowed. Only Active Fellows of the American Medical Golfing Association may compete for prizes. No trophy is awarded a Fellow who is absent from the annual dinner.

MEDICAL LEGISLATION

MEDICAL BILLS IN CONGRESS

Change in Status.—H. R. 6730 has been reported to the House, without amendment, proposing to regulate the mail order business in dentures.

Bills Introduced.—S. 2270, introduced by Senator Green, and H. R. 6701, introduced by Representative Forand, both of Rhode Island, propose to amend the Social Security Act so as to provide federal grants to states for war displacement assistance, for special wartime assistance and for other general public assistance. The purpose of the bills is to provide security (1) for workers unemployed because of priorities and the conversion of industries to war production, (2) for persons in need because of other wartime conditions and (3) for other persons in need. S. 2320, introduced by Senator Downey, California, provides that all persons engaged in civilian defense duty under the laws of the United States or of any state, or political subdivision thereof, who sustain disease or injury while in the lawful performance of such duty shall be paid by the United States monthly compensation for such disease or injury. S. 2335, introduced by Senator Stewart, Tennessee, proposes a federal appropriation in such amount as may be necessary to enable each state to furnish financial assistance to needy individuals who are permanently and totally disabled. S. 2371, introduced by Senator Tunnell, Delaware, proposes to regulate the mail order business in dentures. This bill is similar to H. R. 6730, which has already been reported to the House, as already indicated. H. R. 6710, introduced by Representative Martin J. Kennedy, New York, proposes to amend the Soldiers' and Sailors' Relief Act of 1940 so as to waive the collection of any income tax in the event that the taxpayer dies while in military service. H. R. 6744, introduced by Representative Collins, Mississippi, proposes to extend the benefits of the Social Security Act now applicable to the blind to persons permanently crippled to a degree which renders them unable to engage in a gainful occupation.

STATE MEDICAL LEGISLATION

Kentucky

Bill Introduced.—H. 335, to amend the premarital physical examination law, proposes to authorize the required examination to be made by physicians of an army medical department or by physicians in an adjoining state, if the adjoining state also requires a premarital examination for the presence of syphilis.

Bill Enacted.—H. 315 exempts from the operation of the uniform narcotic act the "administering, dispensing or selling at retail of any medicinal preparation that contains in 1 fluidounce or, if a solid or semisolid preparation, in 1 avoirdupois ounce, not more than 1 grain of codeine or any of its salts." The former law also exempted from the operation of the act the prescribing, administering, dispensing or selling at retail of any medicinal preparation that contains in 1 fluidounce, or, if a solid or semisolid preparation, in 1 avoirdupois ounce, not more than 2 grains of opium, not more than ¼ grain of morphine or any of its salts, not more than 1 grain of codeine or any of its salts, not more than ⅛ grain of heroin or any of its salts, and not more than one of any of said drugs.

Michigan

Bills Enacted.—H. 15-XX authorizes the state commissioner of health to manufacture or purchase antitoxin, sulfonamides, biologic products, silver nitrate ampules, arsphenamines and heavy metals and to furnish them to health officers and health boards, county hospitals and municipal hospitals of the state for use in the control of communicable diseases. H. 16-XX requires physicians to report all cases of venereal diseases coming under their professional observation. The state health commissioner is authorized to make rules and regulations for the care, treatment, hospitalization and isolation of persons afflicted with venereal diseases, but such persons shall have the right to select the physician or mode of treatment of his choice.

Mississippi

Bills Introduced.—H. 738, to amend the law relating to the sale of eyeglasses, proposes to make it an unlawful act for any physician or surgeon to advertise in any manner, either directly or indirectly, any fraudulent, false or misleading statement as to the skill or method of practice of himself or of any other physician or surgeon, or to advertise in any manner that will tend to deceive, mislead or defraud the public. H. 135, to regulate and define the practice of cosmetic therapy and to provide for the administration of said act, proposes to authorize the creation of a board of cosmetic therapy to examine and license persons desiring to practice that art. Cosmetic therapy or beauty culture as defined by this act would include, among other things, the following: "and/or with hands or mechanical or electrical apparatus or appliances, . . . massaging, cleansing, stimulating, manipulating, exercising, beautifying, or similar work, on the scalp, face, neck, arms, bu t, or any part of the body, . . ." H. 766 proposes to provide for the commitment, custody, maintenance and discharge of insane persons and proposes that persons may be adjudged insane on a certificate of lunacy made by two qualified examiners, who should be physicians.

Bill Enacted.—S. 152, to amend the pharmacy act, provides that persons formerly licensed as an assistant pharmacist who had been engaged in practice as an assistant pharmacist for a period of five years shall be licensed to practice pharmacy on passing the required examination and furnishing satisfactory evidence of education and other qualifications. The act further provides that this special provision allowing the granting of a full license to assistant pharmacists shall be in force only during the national emergency proclaimed by the President of the United States and for six months thereafter.

New Jersey

Bills Introduced.—A. 170 proposes the creation of a state eugenic commission and the appointment of a state eugenist and declares it to be the policy of the legislature to ameliorate the living conditions of afflicted individuals and to promote the social welfare by the sexual sterilization, either voluntary or compulsory, of persons suffering from mental deficiency, familial mental disease, familial epilepsy, familial blindness, familial deafmutism, familial gross deformity and familial neurological disease. Mental deficiency is defined by the act as "an irremediable arrest of brain development producing such lack of intelligence as results in social incompetence." A. 171 proposes that any inmate of an institution within the jurisdiction or control of the department of institutions and agencies who shall be so afflicted as to come within the provisions of any law of the state requiring voluntary or compulsory sterilization shall not be permitted to leave such institution until he shall have been subjected to such sterilization treatment as the law shall require.

New York

Bills Introduced.—S. 1210 and A. 1403, to amend the education law, propose to change the filing fees for professional licenses in New York City from $1 to $2 to make it accord with fees imposed for other services. A. 1267, previously reported, has been amended by the assembly so that its terms should apply to "any public hospital in the state" rather than "to any hospital of the state" as provided in the original bill. A. 1434, to amend the education law, proposes the creation of a state board of chiropractic examiners to examine and license applicants desiring to practice chiropractic in the state. The practice of chiropractic is defined as the science of locating and the removing of nerve interference in the human body, according to chiropractic principles, where such interference is indicated or misalinement or subluxations of the vertebral column appear. It excludes operative surgery, the reduction of fractures, the prescription or use of drugs or medicine, and the practice of obstetrics.

Bill Enacted.—S. 100, to amend the public health law, provides for the furnishing of hospital or institutional care under the surveillance of the local health officer at the expense of the state to individuals declared by the state commissioner of health to be carriers of typhoid fever bacilli.

Pennsylvania

Bill Introduced.—S. 41, to amend the unemployment compensation act, proposes among other things to exempt from the operation of the act services performed by a student nurse in the employ of a hospital or a nurses' training school by an individual who is enrolled and is regularly attending classes in a nurses' training school chartered or approved pursuant to the laws of this commonwealth and services performed by an intern in the employ of a hospital by an individual who has completed a four years course in a medical school chartered or approved pursuant to the laws of this commonwealth.

Rhode Island

Bills Introduced.—H. 819, to amend the factory law, proposes to require all companies operating any mechanical establishment where machinery is used for manufacturing to maintain fully equipped at all times a modern medical or surgical chest which shall contain plasters, bandages, absorbent cotton, gauze, antiseptics, ointments, medicine, equipment, first aid instruments and appliances necessary to render adequate first aid treatment to persons injured or taken ill on the premises. The bill further proposes that any firm or corporation employing 100 persons or more shall set aside a special accident room under the supervision of a registered nurse who has taken special courses in first aid treatment from some recognized educational institution or hospital or the American Red Cross that shall meet with the approval of the director of health.

Virginia

Bills Introduced.—S. 268, to amend the narcotic drug act, proposes to exempt from the application of the act the administering, dispensing or selling at retail of any medicinal preparation that contains in 1 fluidounce, or, if a solid or semisolid preparation, in 1 avoirdupois ounce, not more than 1 grain of codeine or of any of its salts. The present law also exempts from the application of the act certain preparations containing opium, morphine and heroin as well as codeine.

Bills Passed.—The following bills have passed the Senate: S. 189, to amend the medical practice act, proposes to authorize the state board of medical examiners to admit to examination all applicants who have completed in not less than thirty-two months the four courses of at least eight months each required by the present law. Under the present law such four courses must have been given in four different calendar years. S. 219, to amend the law relating to the sale of certain hypnotic drugs, proposes that the term "dangerous drug" shall include, in addition to those covered by the present law, the following: "Sulfanilamide (para-amino-benzene-sulfonamide), Sulfathiazole, Sulfapyridine, Sulfadiazine, Sulfaguanidine and any Sulfanilamide derivatives by whatsoever trade name or designation; or any related compound, preparation, mixture or salt thereof; or any salt or derivative thereof; or any preparation or mixture containing any of them." These drugs may be sold only on a physicians' prescription, which may not be refilled except in the case of persons suffering from chronic afflictions or diseases. The following bill has passed the house: H. 421, to amend the alcoholic beverage control act, proposes that alcoholic beverages may be sold only in drug stores, only for medicinal purposes and only on a physician's written prescription.

Bills Enacted.—S. 110 increases the per diem fee to be received by members of the board of medical examiners except the secretary from $8 to $10 and increases the maximum salary which the secretary may be allowed from $1,000 to $1,500. S. 113 provides that no person shall sell any patent, proprietary or domestic medicines, salve, liniment or compounds of a like kind, or any spices, or extracts, toilet articles or other articles of like kind without a license. Exempted from the operation of this act are licensed merchants but not licensed physicians. S. 120 provides that no institution of learning in the state of Virginia shall confer any college degree, whether academic, professional or honorary, unless and until such institution has been approved for such purpose by the state board of education. This act does not apply, however, to an institution of higher learning accredited by the state board of education for granting of college degrees or specifically authorized by an act of the general assembly.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEM OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ADDITIONAL MEDICAL COLLEGE NEWS AND ARTICLES APPEAR IN THE STUDENT SECTION, PAGE 1017.

CALIFORNIA

Dr. Brunn Honored.—Pupils and friends of Dr. Harold Brunn, clinical professor of surgery, University of California Medical School, San Francisco, have collaborated in a book entitled Medico-Surgical Tributes to Harold Brunn, which has just been published. The foreword is written by Robert Gordon Sproul, president of the University of California, and the preface, by Dr. Langley Porter, dean emeritus of the medical school. Dr. Brunn graduated at the University of Pennsylvania School of Medicine, Philadelphia, in 1895. He has been associated with California since 1898.

The Lane Lectures.—The Stanford University School of Medicine, San Francisco, announces the sixtieth course of popular medical lectures to be given at Lane Hall by the following San Francisco physicians:

Dr. John R. Upton, The Blood Bank: Its Purpose and Uses in War Time, April 3.
Dr. Anthony John J. Rourke, Medical Aspects of Civilian Defense, April 17.
Dr. Henry W. Newman, Alcohol in Relation to Driving Hazards, May 1.
Dr. Charles W. Barnett, Control of Venereal Disease Under War Conditions, May 15.

All are of San Francisco.

Examination for Consulting Psychiatrist.—The California State Personnel Board announces that an examination will be held to fill a position as consultant psychiatrist in the state department of social welfare. Applications must be filed by March 31. Candidates who are successful in the examination must secure a license to practice medicine in California before they can be considered eligible for appointment. They must also have five years' experience in psychiatric therapy, two years of which must have been full time in a child guidance clinic or in some other form of preventive mental hygiene with children in an agency regularly employing full time services of a psychologist and psychiatric social worker. Headquarters will be in Sacramento, but considerable traveling throughout the state is required. The entrance salary will be $400 a month. Communications should be sent to the state personnel board at Sacramento.

CONNECTICUT

School Health Education Conference.—"How the Schools May be Alert to Service in the Present Defense Emergency" will be the theme of a statewide school health education conference in West Hartford, March 24, under the auspices of the state department of health, state department of education and the Connecticut Tuberculosis Association. Section meetings on physical fitness, nutrition and health policies and practices will open the conference. Two general sessions will follow. The speakers will include Neils P. Neilson, A.M., Washington, D. C.; Drs. Creighton Barker, New Haven; Harry E. Kleinschmidt, New York; Charles C. Wilson, New York, Ira V. Hiscock, C.P.H., New Haven, and Mrs. Chase Going Woodhouse, Hartford, secretary of state.

DISTRICT OF COLUMBIA

Interprofessional Society Organized.—The Medical Society of the District of Columbia recently sponsored the organization of the Interprofessional Conference to discuss mutual problems of the pharmaceutic, dental and nursing professions; hospital representatives also are included. Dr. Robert Lomax Wells was elected chairman of the conference and Mr. Theodore Wiprud, secretary of the medical society, secretary. Each professional group alternately acts as host at meetings.

The Food Front.—A series of lectures on the Food Front opened, March 11, in the U. S. Department of Agriculture Auditorium, Washington, to continue through April 15. Paul V. McNutt, administrator, Federal Security Agency, and director of the Office of Defense Health and Welfare Services, and Craig McGeachy, public relations officer, British embassy, gave the first two lectures, on "The National Nutrition Program" and "What the War Has Taught Us About Food" respectively. On March 18 Dr. Thomas Parran, surgeon general, U. S. Public Health Service, spoke on "Nutrition and Public Health" and Paul Cornell, consultant, Nutrition Division, Office of Defense Health and Welfare Service, "Factors Affecting Public Acceptance of the Nutrition Program." The rest of the series follows:

Hazel K. Stiebeling, Ph.D., senior food economist, Bureau of Home Economics, Department of Agriculture, How Well Fed Is the American Family? March 25.
Dr. Martha M. Eliot, associate chief, Children's Bureau, Department of Labor, Nutrition and the Child, March 25.
Esther L. Batchelder, Ph.D., chief, Foods and Nutrition Division, Bureau of Home Economics, Department of Agriculture, Conserving the Foods We Produce, April 1.
Eugene C. Auchter, Ph.D., Agricultural Research Administration, Department of Agriculture, Interrelationship of Soil, Plant and Human Nutrition, April 1.
Claude R. Wickard, Secretary of Agriculture, Food Production Goals, April 8.
R. B. Brand, head, British Food Mission in North America, The British Food Supply, April 15.
Dr. Frank G. Boudreau, New York, chairman, Food and Nutrition Board, National Research Council, Present and Future Food Supply and Some International Implications, April 15.

ILLINOIS

Annual Lecture of Springfield Club.—Dr. Perrin H. Long, Baltimore, delivered the tenth annual lecture of the Springfield Medical Club in Springfield, March 18, on "The Latest Aspects of Sulfonamide Therapy."

District Meeting.—The spring meeting of the Iowa and Central District Medical Association will be held at the Fort Armstrong Hotel in Rock Island, March 26. Dr. Robert Lee Sanders, associate professor of surgery, University of Tennessee College of Medicine, Memphis, as guest speaker will discuss "Surgical Lesions of the Colon." Dr. Florian E. Schmidt, Chicago, of the Lederle Laboratories, will show a motion picture in color with sound on "All Sulfonamide Therapy."

Chicago

Course in Neuromuscular Anomalies of the Eyes.—The eighth semiannual postgraduate course in muscles of the eyes will be given at the Children's Memorial Hospital, May 3-8. The lectures will be given by Dr. George P. Guibor. The courses will include lectures and clinical demonstrations of muscle defects of the eyes. Inquiries regarding the course may be addressed to the hospital, 707 Fullerton Avenue.

Society News.—At a meeting of the Chicago Gynecological Society, February 21, Dr. George F. Pendleton, Kansas City, Mo., spoke on "Maternal Health in Kansas City"; Dr. James F. Nolan, St. Louis, and Dr. Axel N. Arneson, St. Louis, "The Use of Radium in the Treatment of Corpus Cancer."—The Chicago Urological Society was addressed, February 26, by Dr. Walter G. Sexton, Marshfield, Wis., on "Cortical Hypernephroma"; Dr. Leslie L. Veseen, lieutenant commander, U. S. Navy, "Urological Routine in the Navy"; Drs. Harry C. Rolnick and Israel Davidsohn, "Involvement of the Kidney in Periarteritis Nodosa," and Dr. Russell D. Herrold, "Failures and Problems of Chemotherapy in Urology."

IOWA

Regional Meeting on Physical Therapy.—The spring session of the Midwestern Section of the American Congress of Physical Therapy will be held at the University Hospitals, Iowa City, April 6. The following program will be presented:

Dr. Stuart C. Cullen, Iowa City, The Rationale of Oxygen Therapy During Hyperpyrexia.
Dr. Max K. Newman, Detroit, Hypothermic Anesthesia in Extremity Surgery.
Adelaide P. Barer, Ph.D., Iowa City, The Effect of Ultraviolet Irradiation on Hemoglobin Formation.
Dr. John S. Coulter, Chicago, Physical Therapy in Fractures.
Dr. Arthur Steindler, Iowa City, The Treatment of Acute and Subacute Poliomyelitis.
Dr. Frank H. Krusen, Rochester, Minn., The Relation of Physical Therapy in War.

State Medical Meeting.—The ninety-first annual session of the Iowa State Medical Society will be held at the Hotel Fort Des Moines, April 15-17, under the presidency of Dr. Earl B. Bush, Ames. The guest speakers will include:

Dr. John A. Toomey, Cleveland, Differential Diagnosis of Meningeal Irritations.
Dr. James T. Priestley, Rochester, Minn., Carcinoma of the Stomach.
Dr. Sumner L. S. Koch, Chicago, Treatment of Raw Surfaces Resulting from Burns and Injuries.
Dr. John L. McKelvey, Minneapolis, Cesarean Section.
Dr. French K. Hansel, St. Louis, Allergy.
Dr. Oscar B. Nugent, Chicago, Newer Methods of Treating Strabismus.
Dr. Reginald Fitz, Boston, Certain Peculiarities of Gallstone Disease.
Dr. William R. Cubbins, Chicago, Fractures Around the Knee Joint.

There will be general sessions, sectional meetings and clinics, with Iowa physicians participating. One general session will be devoted to a symposium on injuries, to be followed by an address on the "Procurement and Assignment of Physicians" by Major Sam F. Seeley, M.D., Washington, D. C. The Iowa Orthopedic Club, the Iowa State Pediatric Society, the State Society of Iowa Medical Women and the American Medical Women's Association, branch 19, are among the groups that are also planning meetings at this time. The woman's auxiliary to the state medical society will hold its thirteenth annual meeting at the Hotel Kirkwood, April 15-16.

MICHIGAN

Increase in Biologic Products.—The state health department has announced that a 10 per cent increase in the distribution of biologic products was noted in 1941 as compared with 1940. These included vaccines against smallpox, diphtheria and whooping cough, antitoxins and serums, all produced in the state department laboratories at Lansing. The department reported that vaccines, serums and other biologic products distributed free to physicians in 1941 reached an all time high of 2,499,618 doses.

Changes in Health Personnel.—Dr. Henry G. Steinmetz, Flint, health commissioner of Genesee County, has been appointed assistant director to the bureau of venereal diseases in the state department of health. Dr. Lars W. Switzer, Cassopolis, health officer of Cass County, will serve as health officer until the return of Dr. Leslie V. Burkett, Flint, in June. Dr. George F. Moench has been appointed director of the Calhoun County Health Department, Marshall, succeeding Dr. Hugh B. Robins, who is on leave doing graduate work at the University of Michigan School of Hygiene and Public Health. Dr. Moench was formerly director of the Delaware County Health Department, Delaware, Ohio.

NEBRASKA

Contest on Biography of Pioneer Physician.—The Native Sons and Daughters of Nebraska is sponsoring a contest on the biography of a pioneer Nebraska physician. According to the rules of the contest a pioneer is "any one engaged in the practice of medicine within the present boundaries of the state prior to 1890, or within the first twenty years of a community's life." The essay must not be longer than four thousand words. Any Nebraska resident is eligible. The time limit is June 30.

NEW JERSEY

Forty-Three Years as Health Officer.—Dr. Alton S. Fell, health officer of Trenton for forty-three years, retired on March 1. Dr. Fell graduated at Hahnemann Medical College and Hospital of Philadelphia in 1894.

Society News.—Dr. Oswald S. Lowsley, New York, discussed "Recent Advances in Modern Urology" before the Essex County Medical Society, March 12.——The Gloucester County Medical Society was addressed, February 19, by Dr. Joseph C. Yaskin, Philadelphia, on "The Neuroses from the Standpoint of the General Practitioner."——The Camden County Medical Society meeting, February 3, was addressed by Dr. Jonathan E. Rhoads, Philadelphia, on "Newer Concepts of Liver Disease."——Dr. John Scudder, New York, addressed the Morris County Medical Society, February 19, Greystone Park, on "The Modern Treatment of Shock."

NEW YORK

Bacteriologist Granted Leave for Latin American Survey.—Robert S. Breed, Ph.D., chief in research bacteriology, New York State Agricultural Experiment Station at Geneva since 1913, has been granted a leave of absence to conduct a survey of dairy research and education in South America for the Inter-American Committee for the Dairy Industry, according to *Science*. Dr. Breed received his doctor of philosophy degree at Harvard University in 1902. He served as vice president of the World Dairy Congress at Washington-Syracuse, 1923, and London, 1928. He was chairman of the laboratory section of the American Public Health Association in 1934.

Youth Educational Program.—The Health Division of the National Youth Administration and the state department of health have arranged a program of health education in fifteen NYA resident centers and thirty-five nonresident workshops throughout the state, supplementing the regular health program of the administration. The primary object of the program is to make a physical study and appraisal of each youth through a competent over-all medical examination and, with the cooperation of the health agencies and through counseling with youths, to effect correction of physical defects and rehabilitation of those requiring special medical services. Competent speakers and supplementary educational material will be available. In the educational project emphasis will be placed on information regarding tuberculosis, venereal disease, accidents and nutrition.

New York City

Alumni Meeting.—The Cornell University Medical College Alumni Association will hold its annual meeting at the college, April 16, when a scientific program will be presented. A banquet will be held in the evening at the Waldorf-Astoria.

The Miller Memorial Lecture.—Dr. Eliot Round Clark, professor of anatomy, University of Pennsylvania School of Medicine, Philadelphia, delivered the sixth Adam M. Miller Memorial Lecture at the Long Island College of Medicine, January 16. His subject was "The Behavior of Cells and Tissues in the Living Mammal as Observed Through the Microscope."

Clinical Session on Pulmonary Diseases.—Dr. Lloyd F. Craver of the Memorial Hospital for the Treatment of Cancer and Allied Diseases conducted a symposium on "Pulmonary Tumors in Persons Under Thirty Years of Age" at the twenty-ninth clinical session on chronic pulmonary diseases, February 11. Preceding the meeting there was a presentation and discussion of x-ray films.

Courses in Gastroenterology and Cardiovascular Diseases.—Two full time courses of four weeks each in gastroenterology and cardiovascular diseases will be held at Mount Sinai Hospital, April 6-May 2, in cooperation with Columbia University. Additional information may be obtained from Edith Levy, secretary for medical instruction, Mount Sinai Hospital, Fifth Avenue and One Hundredth Street.

Program on Sulfonamides.—The New York Branch of the American Pharmaceutical Association held a special meeting, February 9, at the Columbia College of Pharmacy, to discuss "The Sulfonamides." The speakers included Curt P. Wimmer, Ph.M., on "The Pharmacology of the Sulfonamides"; Dr. Salo N. Weber, "Sulfonamides in the Treatment of Pneumonia"; Dr. Adolph Jacoby, "Sulfonamides in the Treatment of Gonorrhea and the Venereal Diseases," and Dr. Maurice J. Costello, "Sulfonamides in Treatment of Disease of the Skin."

Friday Afternoon Lectures.—The Medical Society of the County of Kings, Brooklyn, opened a series of Friday afternoon lectures and Monday panel discussions with a talk by Dr. Gregory L. Robillard, March 6, on "Tumors of the Breast." The entire program of lectures is as follows:

Dr. Albert F. R. Andresen, Diarrheas in Adults, March 13.
Dr. Meyer A. Rabinowitz, Thrombosis-Embolism and Thrombophlebitis, March 20.
Dr. Louis Chargin, New York, Massive Dose of Arsenotherapy for Syphilis, March 27.
Dr. Eugene R. Marzullo, Transfusions, April 10.
Dr. Wheelan D. Sutliff, New York, Sulfa Compound Therapy, April 17.
Dr. Thurman B. Givan, Diarrheas in Infancy and Childhood, April 24.

On the Monday following the lecture a panel discussion was held on the subject.

PENNSYLVANIA

Society News.—The Pennsylvania Psychiatric Society held its third midyear meeting at the Harrisburger Hotel, Harrisburg, February 10. Dr. Winfred Overholser, Washington, D. C., spoke on "Some Possible Contributions of Psychiatry to the National Defense."——Dr. Clay Ray Murray, New York, discussed "Problem Fractures of the Upper Extremity for the General Practitioner" before the Lycoming County Medical Society, March 13, in Williamsport.

Philadelphia

Special Lectures.—Dr. Edward B. Krumbhaar, professor of pathology, University of Pennsylvania School of Medicine, delivered a public lecture for the College of Physicians of Philadelphia, March 20. His subject was "Superstition and Medical Progress." Dr. Charles Sidney Burwell, dean and research professor of clinical medicine, Harvard Medical School, Boston, will deliver a Mary Scott Newbold Lecture, May 6, on "Studies of the Circulation in Congenital Affections of the Heart and Their Application to Some of the Problems of Heart Disease."

Pharmaceutic Seminar.—The fourth annual seminar on modern pharmaceutic practice will be conducted by the Philadelphia College of Pharmacy and Science, April 6-9. Heretofore the seminar has been of three days' duration, but the national emergency has prompted the college officials to extend

the seminar one additional day to include an official standard Red Cross first aid course. In addition to the first aid instruction, members of the faculty will lecture on such subjects as pharmaceutic economics in war times, the pharmacist's part in war gas defense and the chemistry, pharmacy and therapeutics of the new drugs of the Pharmacopeia which soon becomes official.

Annual Postgraduate Institute.—The Seventh Annual Postgraduate Institute of the Philadelphia County Medical Society will be held at the Bellevue-Stratford Hotel, April 13-17. A symposium on modern therapy will constitute the program. Included among the speakers will be:

Dr. Thomas Grier Miller, The Significance of Nutrition in Relation to National Defense.
Thomas J. Cook, D.D.S., Mouth Lesions Due to Non-Nutritional Disturbances.
Dr. George Harlan Wells, Diabetes Complicated by Tuberculosis.
Dr. James M. Surver, Surgical Emergency Operations on the Diabetic.
Dr. Charles C. Wolferth, The Management of Coronary Disease in the Diabetic.
Dr. Harrison F. Flippin, Recent Advances in Sulfonamide Therapy.
Dr. John S. Lockwood, Surgical Importance of Chemotherapy.
Dr. Bernard J. Alpers, Chemotherapy of Infections of Central Nervous System.
Dr. William G. Leaman Jr., The Management of the Cardiovascular Complications of Anemia and the Deficiency Diseases.
Charles Wesler Scull, Ph.D., Elkins Park, Pa., Pathology and Metabolism of the Arthritides in Relation to Therapy.
Dr. William I. Westcott, Doylestown, Pa., Chemotherapy (Gold) and Endocrine Therapy.
Dr. Morris A. Bowie, Bryn Mawr, Pa., The Use and Abuse of Analgesic Drugs: Indications for and Effects of Physical Therapy.
Dr. Ralph Pemberton, Effective Organization of the Treatment of Arthritics.

Pittsburgh

Stewart Memorial Lecture.—The annual R. W. Stewart Memorial Lecture was delivered in the Pittsburgh Academy of Medicine, March 10, by Dr. Isidor S. Ravdin, George Leib Harrison professor of surgery, University of Pennsylvania School of Medicine. His subject was "Biliary Tract Disease."

SOUTH CAROLINA

Society News.—Dr. Arthur Bruce Gill, Philadelphia, discussed "The Etiology and Treatment of Chronic Backache, with Particular Reference to the Effect of Postural Defects" before the Columbia Medical Society in Columbia, February 9, and Dr. George H. Bunch, Columbia, spoke on "Postoperative Tetanus."——The Marlboro County Medical Society was addressed in Bennettsville, January 7, among others, by Dr. Frank A. Hoshall, Charleston, on "Fractures of the Wrist from the Industrial Standpoint."

Tri-State Associations' New Officers.—Dr. Frank S. Johns, Richmond, Va., was chosen president-elect of the Tri-State Medical Association of the Carolinas and Virginia at its meeting in Greenville, February 23-24, and Dr. George R. Wilkinson, Greenville, was installed as president. Vice presidents are Drs. Walter B. Martin, Norfolk, Va.; Karl B. Pace, Greenville, N. C., and Clay W. Evatt, Charleston, S. C. Dr. James M. Northington, Charlotte, N. C., was reelected secretary-treasurer. The 1943 meeting will be held in Lynchburg, Va.

UTAH

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Utah are required to register annually on or before April 1 with the state department of registration and to pay a fee of $3. If a licentiate fails to reregister within ninety days to six months after April 1 his license can be revoked and, if revoked, it will be reinstated thereafter only on his paying the delinquent registration fees and an additional year's fee as a penalty.

WASHINGTON

Dr. Loewi Appointed to Special Professorship.—Dr. Otto Loewi, research professor of pharmacology at New York University, New York, has been appointed Walker-Ames professor of pharmacology and physiology at the University of Washington, Seattle, for the spring quarter. He will conduct a series of weekly seminars on Tuesday evening, beginning April 14, on the following topics: "The Point of Attack of Autonomic Drugs," "Specific Sensitivity and Hypersensitivity of Denervated Organs," "The Action of Cations," "Problems Connected with the Chemical Transmission of the Nervous Impulse," "Blood Sugar Regulation" and "Questions Related to Hormone Action." Four general lectures, open to the public, will be given as follows: "The Story of the Chemical Mediation of Nervous Activity," April 22; "Drug Action and Drug Discovery," May 6; "Adaptation and Regulation Within the Organism," May 20, and "The Organism as a Unit," May 27.

WYOMING

Annual Registration Due April 1.—All practitioners of medicine and surgery licensed to practice in Wyoming are required by law to register on or before April 1 with the secretary of the board of medical examiners and to pay a fee of $2.50. If a licentiate fails to pay the fee within three months after April 1, his license can be annulled, and, if annulled, it will be reinstated only on his paying the stated fee plus $5 as a penalty.

GENERAL

Thoracic Surgeons Cancel Meeting.—The annual meeting of the American Association for Thoracic Surgery, planned for St. Louis May 13-16, has been canceled on account of the war.

Change in Ophthalmology Meeting.—The American Academy of Ophthalmology and Otolaryngology will meet in Chicago, October 11-14, instead of San Francisco as was previously announced. The convention period has been shortened one day, consolidating five days' activities into four.

Applications for Grants for Research—The Committee on Scientific Research of the American Medical Association invites applications for grants in support of researches on problems more or less closely connected with clinical medicine and public health. For information address the committee at 535 North Dearborn Street, Chicago.

Doctor Needed in Peru.—The Peruvian Inland Mission is urgently in need of a doctor for its hospital at Lamas, Province of San Martin. The director of the mission is Miss Annie G. Soper. The Peruvian government offers the post of "Medico Titular" to a physician who can use Spanish and who is willing to have his medical practice certificate revalidated at an outlay of approximately $400. The position of "Medico Titular" carries a monthly salary of $80. Since the work is under a faith mission, it is desired that the applicant be one who comes in a spirit of religious devotion. Apply to Dr. Edward H. Hume, 156 Fifth Avenue, New York.

Contest for the Design of an Emblem.—The American Psychiatric Association has announced a contest for the design of an emblem to be used in the centennial celebration of the association in 1944. Five hundred dollars is available for prizes. Artists, art teachers and students are invited to compete, the drawings to reach the association not later than April 15. Literature to assist in forming a background for the design may be obtained from Dr. Gregory Zilboorg, 14 East Seventy-Fifth Street, New York. Information concerning administrative matters may be obtained from Mr. Austin Davies, executive secretary of the association, 9 Rockefeller Plaza, New York.

Association of Medical Museums.—The thirty-fifth annual meeting of the International Association of Medical Museums will be held at the Washington University School of Medicine, St. Louis, April 1, under the presidency of William H. Feldman, M.S., Rochester, Minn. The headquarters will be at the Chase Hotel. After a business session the program will open with a symposium on comparative pathology. Among the speakers will be: Dr. William O. Russell, St. Louis, on "Experience with Plastic Cover Slips"; Dr. Emmerich von Haam and Mary R. Schuh, Columbus, Ohio, "Cytologic Studies with the Electron Microscope"; Dr. Jacob Werne, Jamaica, New York, "Postmortem Incidence of Tuberculosis in a Population Dying of Violence as Determined by X-Ray and Mechanical Slicing of the Lungs," and Dr. Robert A. Moore, St. Louis, "Rubber Autopsy Sheet."

Meeting of Pathologists and Bacteriologists.—The forty-second annual meeting of the American Association of Pathologists and Bacteriologists will be held at the Washington University School of Medicine, St. Louis, April 2-3. Among the speakers will be:

Clarence C. Lushbaugh, Ph.D., and Dr. Paul E. Steiner, Chicago, Fatal Maternal Pulmonary Embolism by Amniotic Fluid.
Dr. Edward Smith, St. Louis, Fibrous Pleural Adhesions.
Drs. James W. Logie and Carl V. Weller, Ann Arbor, Mich., Statistical Investigation of the Correlation Between Mastopathia Cystica and Mammary Cancer.
Dr. Elexious T. Bell, Minneapolis, The Vascular Changes in the Kidney in Diabetes Mellitus.
Dr. Howard C. Hopps, Chicago, Allergic Reactions to Surgical Catgut—An Experimental Study.
Dr. Jacob Werne, Jamaica, N. Y., Postmortem Evidence of Acute Infection in Unexpected Death of Infancy and Childhood.
Dr. Howard T. Karsner, Cleveland, General Considerations of Functioning Tumors of Endocrine Glands.
Drs. Ernest M. Hall and Lucile R. Anderson, Los Angeles, The Incidence of Rheumatic Stigmas in Nonrheumatic Hearts.

American Surgical Association.—The annual convention of the American Surgical Association will be held at the Cleveland Hotel, Cleveland, April 6-8, under the presidency of Dr. Harvey B. Stone, Baltimore. The tentative program includes the following speakers:

Drs. William A. Altemeier Jr. and Burr N. Carter, Cincinnati, Chronic Infected Burns with Hemorrhage.
Dr. Albert O. Singleton, Galveston, Texas, The Problem of Intestinal Gases Complicating Abdominal Surgery.
Dr. Owen H. Wangensteen, Minneapolis, New Operative Technics in the Management of Bowel Obstruction.
Dr. Roscoe R. Graham, Toronto, Ontario, Canada, The Operative Repair of Massive Rectal Prolapse.
Drs. Andre Cournand and Francis B. Berry, New York, Effect of Pneumonectomy on Cardiac Pulmonary Function in Adults.
Dr. Charles B. Huggins, Chicago, Treatment of Metastatic Cancer of the Prostate.
Drs. Isidor S. Ravdin and Henry P. Royster, Philadelphia, Reflexes Originating in the Common Duct Giving Rise to Pain Simulating Angina Pectoris.
Dr. John C. Burch and Doris H. Phelps, Ph.D., Nashville, An Experimental Approach to the Problem of Menstrual Disorders.
Dr. Cecil K. Drinker, Boston, Use of Oxygen in the Treatment of Transudation and Exudation into the Lungs.

Congress on Obstetrics and Gynecology.—The second American Congress on Obstetrics and Gynecology will be held at the Municipal Auditorium in St. Louis, April 6-10, under the general chairmanship of Dr. Fred L. Adair, Chicago. One session of the medical section will be devoted to "The Obstetric Use of Vitamin K." Another will be on the endocrines. General sessions will cover chemotherapy, shock and hemorrhage, control of eclampsia, genital cancer and the economics of obstetric care. Evening meetings will be addressed, among others, by Dr. Joseph G. Hamilton, San Francisco, on "Biologic and Medical Applications of Nuclear Physics"; Logan Clendening, Kansas City, Mo., "The Place of Obstetrics in the Various Epochs of the History of Mankind," and Arthur C. Corcoran, Indianapolis, "Renal Aspects of Hypertensive and Eclamptogenic Toxemia." Included among the speakers on the program will be the following:

Edward A. Doisy, Ph.D., St. Louis, Chemistry and Action of Vitamin K.
Dr. Alexander E. Brown, Rochester, Minn., History and Pharmacologic Aspects of Chemotherapeutic Drugs.
Dr. Lawrence M. Randall, Rochester, Minn., Gonadotropic Hormones.
Dr. Frank W. Hartman, Detroit, Physiology and Pathology of Shock and Hemorrhage.
Dr. Madge T. Macklin, London, Ontario, Canada, Heredity as an Etiologic Factor in Genital Cancer.

One combined session will be held by the medical and educators sections for a study of sterility and infertility. Round table discussions will form a large part of the program.

Association of Anatomists.—The fifty-eighth annual session of the American Association of Anatomists will be held at Cornell University Medical College and the Hotel Commodore, New York, April 1-3, under the presidency of Philip E. Smith, Ph.D., New York, whose address will be "Some Aberrant Responses to Sex Hormones." The program includes the following speakers:

Melvin H. Knisely, Ph.D., Chicago, and Edward H. Bloch, B.S., Memphis, Tenn., Microscopic Observations of Intravascular Agglutination of Red Cells and Consequent Sludging of the Blood in Human Diseases.
Edmond J. Farris, Ph.D., Philadelphia, The Blood Picture of Athletes as Affected by Intercollegiate Sports.
Edgar Allen, Ph.D., New Haven, Further Studies of the Ovaries and Genital Tract At and Shortly After Ovulation.
Frank Harrison, Ph.D., and Dr. Kendall B. Corbin, Memphis, Tenn., Oscillographic Studies on the Spinal Tract of the Trigeminal Nerve.
William H. Whitehead, A.B., Chicago, Changes in Lung Structure During Aspiration of Amniotic Fluid and During Air Breathing at Birth.
Earl W. Count, Ph.D., New York, Growth Pattern of the Human Physique.
Drs. Joseph H. Globus, New York, and Hartwig Kuhlenbeck, Philadelphia, The Subependymal Cell Plate and Its Relation to Brain Tumors of Neuroectodermal Derivation.
Walter A. Stultz, Ph.D., Burlington, Vt., Alterations in the Spinal Cord of Amblystoma Following Changes in the Peripheral Field.
Dr. Joseph Krafka Jr., Augusta, Ga., A Free Human Tubal Ovum in a Late Cleavage Stage.
Albert W. Hetherington, Ph.D., Chicago, The Effect of Early Hypophysectomy on Hypothalamic Obesity.

Latin American Program.—A new division of health and sanitation has been created in the Office of Inter-American Affairs, according to the New York *Times*. Dr. George C. Dunham, director of laboratories, U. S. Army Medical School, Washington, D. C., has been appointed director. He will organize a field staff to carry out whatever arrangements are made between the officials of the United States and the Latin American countries. One project already instituted is a mission to Quito and Guayaquil in Ecuador. According to the *Times* the mission will concentrate on those areas which are considered vital in carrying out the defense of the hemisphere. Included on the staff are Dr. Walter C. Earle, member of the field staff, International Health Division, Rockefeller Foundation, New York, and Wyman Stone, sanitary engineer. Among other projects to be undertaken will be the regulation of water supply, waste disposal systems, the building of hospitals in defense areas and the training of sanitation specialists in the Latin American countries. The program will tie in with the activities of the Pan American Sanitary Bureau, the twenty commissions organized in the other American republics under the Inter-American Development Commission and various private foundations, the *Times* stated.

Society for Pharmacology and Experimental Therapeutics.—The American Society for Pharmacology and Experimental Therapeutics, Inc., will hold its annual meeting in Boston, March 31-April 4, under the presidency of Dr. Eugene M. K. Geiling, Chicago. Among the speakers will be:

Dr. Robert C. Batterman, New York, Effectiveness in Man of Demerol, A New Analgesic Drug.
Dr. Gerhard Katz, New Orleans, Histamine Release in the Allergic Skin Reaction.
Albert J. Plummer, Ph.D., Boston, Antagonism Between Nicotine and Physostigmine.
Dr. Ko Kuei Chen, Indianapolis, and Robert Cobert Elderfield, Ph.D., New York, Unsaturated Lactones Related to Cardiac Glycosides.

On Wednesday there will be a symposium on "Morphine Problems":

Dr. Harold G. Wolff, New York, Pain and Its Relief by Morphine and Related Substances.
Dr. Clifton K. Himmelsbach, Lexington, Ky., Present Status of Morphine Addiction Studies.
Dr. Erwin G. Gross, Iowa City, The Fate in the Body of Morphine and Related Substances.
Dr. Maurice H. Seevers, Ann Arbor, Mich., The Effect of Morphine and Related Substances on Tissue Metabolism.

At a joint symposium of the Federation of American Societies for Experimental Biology five papers will be presented, one from each of the five component societies. Dr. Ralph M. Waters, Madison, Wis., will deliver the paper for the Pharmacology society on "Newer Viewpoints on Clinical Anesthesia." A symposium on "Deficiency Diseases" Friday afternoon will consist of the following:

Charles G. King, Ph.D., Pittsburgh, Pa., Some Specific Physiological Disturbances Induced by Marginal Vitamin Deficiencies (C and B_1).
Franklin C. Bing, Ph.D., Chicago, Food as a Source of Vitamins.
Conrad A. Elvehjem, Ph.D., Madison, Wis., The Biological Action of the Vitamins.
Dr. Hans Molitor, Rahway, N. J., Vitamins as Pharmacological Agents.
Dr. Norman H. Jolliffe, New York, Vitamins in the Practice of Medicine.
Dr. William H. Sebrell Jr., Washington, D. C., Vitamins in Public Health.

LATIN AMERICA

Personal.—Dr. Porter J. Crawford, chief of the health work in Central America, Colombia and Venezuela, of the Rockefeller Foundation, arrived in Nicaragua February 18 to confer with Col. Luis Manuel Debayle, director general of the department of health of Nicaragua, on the organization of medical work in case of a national emergency, according to the New York *Times*.

Society News.—A group of Latin American physicians and scientists met recently in Buenos Aires under the presidency of Dr. Angel H. Roffo, director of the Instituto de Medicina Experimental of Buenos Aires, to organize a Pan American Scientific Confederation for the discussion of scientific Pan American problems.——The eighth Pan American Congress of the Child will meet in Washington, D. C., May 2-9. Miss Katharine F. Lenroot, head of the Bureau of the Child, Washington, D. C., is the president of the organizing committee.

CORRECTIONS

John H. O'Shea.—In THE JOURNAL, February 21, page 638, the name Dr. John M. O'Shea, Spokane, Wash., a member of the Ninth Corps Area committee of Procurement and Assignment, should have been John H. O'Shea.

First Venereal Disease Control Officer in Virginia.—In a news item, February 28, page 745, THE JOURNAL reported that Dr. Aaron Wilson Brown was the first full time venereal disease control officer of Richmond, Va. The announcement was taken from the January issue of the *Virginia Medical Monthly*. Dr. Francis W. Upshur, Williamsburg, Va., writes that he was the first full time venereal disease control officer in the state, serving from April 1, 1938 to April 15, 1940.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Jan. 31, 1942.

The British Medical Students Association

The British Medical Students Association is the latest medical organization formed in this country. It dates only from May 1940, though the National Union of Students had previously a medical subcommittee. But only by means of the association has the corporate voice of medical students been heard for the first time. The outbreak of war produced many difficulties for London medical students. To deal with these, chiefly those concerned with evacuation and air raid precautions, a London medical committee of students was formed, and this body called a general meeting of medical students at Manchester, which set up the British Medical Students Association. The following subjects are now under discussion.

1. Student Health. While the care of student health in a few hospitals, notably University College Hospital, is extremely good, in many hospitals provision for maintaining the student in health is very poor. There is a report from one small teaching hospital of 7 cases of tuberculosis, of which 1 was fatal, in six months. The council of the association unanimously passed a resolution approving of free medical treatment of all students, which should include both medical attendance and hospital accommodation. Every medical student should be examined on entering his school. Examinations should follow at regular intervals and include roentgenography of the chest.

2. Air Raid Precautions and Evacuation. Medical students have a special obligation for air raid precautions and casualties and so were reserved from compulsory military service. There has been considerable friction in fitting the student body into the framework of the local authorities, particularly in the Midlands and the North of England. London students are usually evacuated unless attached to casualty posts. The council holds that teaching standards should be maintained as far as possible in spite of evacuation. To achieve this the hospital system should be more flexible; beds in municipal hospitals should be available for teaching.

3. Medical Education. The Medical Planning Committee of the British Medical Association has invited the British Medical Students Association to state its case. A subcommittee was formed for the purpose and has made the following recommendations: No suitable student should be debarred from medicine for financial reasons, and all schools should be open equally to men and to women. In medical education the emphasis should be on the prevention of disease rather than on the cure. Biology should be taught as a general study of life rather than as a detailed study of a few forms. Chemistry and physics should be taught with more emphasis on general principles. The medical course might be widened to include the elements of anthropology, sociology and genetics. The teaching of anatomy and physiology should be coordinated, with more attention to the developmental approach and to surface anatomy. Clinical cases should be used to illustrate anatomic and physiologic principles. Clinical instruction should be organized for small groups rather than for large classes. Hospital education is not enough; it should be supplemented by a system of apprenticeships to selected general practitioners, or a dispensary system such as operates in some Scottish schools. A state medical examination might replace the various examination standards now existing. There should be a substantial reduction in examination fees.

Some of these reforms have already taken place in certain medical schools. What is entirely new is that medical students should criticize the regulations to which they are subject.

BUENOS AIRES

(From Our Regular Correspondent)

Feb. 1, 1942.

Crusade Against Malaria

A law was passed recently by which malaria is declared a social disease for the control of which all the health centers and authorities should collaborate. The executive power will declare which are the malarial regions of the country. The board of directors of the General Department of Antimalaria Crusade, which is established in Tucumán city as a branch of the Departamento Nacional de Higiene, will establish regional branches and will be in charge of studies and research. The malarial patients who cannot afford medical care and drugs should have both gratis. To facilitate the creation and functioning of new departments in the country and in the small towns with less than five thousand persons, subsidies will be given to provinces and municipalities in the amount of 30 per cent of the total sum of the local budget. There will be a constant and intense crusade for the spreading of education against malaria. The directors of private and official organizations working in malarial regions are obliged to give antimalarial drugs, free of charge, to their employees who have malaria. If the organizations have more than fifty employees the latter should have both medical care and antimalarial drugs gratis. The Departamento Nacional de Higiene will sell antimalarial drugs at low prices to the directors of the organizations. The national department for the control of malaria will carry on work for the destruction of mosquitoes and larvae. Housing in malarial regions is going to be inspected in order to provide the workers with hygienic houses well protected against the entrance of mosquitoes. Factories at a distance of no more than 5 kilometers from small villages have to eliminate stagnant waters. The windows of trains which cross malarial regions should be protected with screens. The owners of farms and industries should make their premises hygienic. If the owners do not institute hygienic measures on their premises after several notifications the place can be closed by order of the government or can be expropriated.

Imported antimalarial drugs will not pay duty. Infraction of the law will be punished. The General Antimalarial Department disposes of a budget of 900,000 Argentine pesos ($225,000) to carry on the antimalarial crusade. The new law will demand great energy from the provincial hygienic authorities. The law provides for an increase of funds for the antimalarial crusade, from 500,000 Argentine pesos in 1907 to 750,000 at the present time ($125,000 and $188,000 respectively). The final plans which aim to suppress endemic malaria will be soon arranged.

Malarial Therapy

A center for malarial therapy was established in 1941 in the Hospicio de las Mercedes in Buenos Aires, a large hospital for the insane. Dr. Gonzalo Bosch is the director of the hospital and Dr. Roque Orlando is director of the malarial center. The strain used at present is the same which was used in 1923 by Drs. Bosch and Mo. It has been maintained at the hospital by means of interhuman transplantations of parasitic blood. The incubation period with this strain varies between five and thirty-five days. The paralytic patients first are treated to improve their general condition. Young trophozoites of Plasmodium malariae, belonging to at least the third malarial attack are used for the intravenous inoculation of malaria for eight or ten malarial attacks. In rare cases six or twelve attacks are provoked. Malaria is then interrupted by administration of quinine sulfate by the mouth. The malarial strain presents a normal schizogonic parasitic morphology. The number of plasmodiums in the peripheral blood is moderate, whereas gametocytes are rarely

observed. The host erythrocytes are not altered. The strain produces no immunity. One or more plasmodial generations can be suppressed by administering from 0.5 to 2 Gm. of quinine sulfate by mouth ten or twelve hours before the appearance of the highest figures of fever in a given attack. Moderate anemia appears during the period of active malarial therapy. There are anisocytosis and poikilocytosis, moderate polychromatophilia and a loss of hemoglobin. These changes do not provoke the appearance of normoblasts or any other signs of sudden regeneration of the blood but they are the cause of the appearance of bilirubinemia. After malarial therapy the erythropoiesis, hemoglobin and leukocytosis became normal. Erythropoiesis improves through functions of the reticulocytes. The increase of the lymphocytes and eosinophils is both relative and absolute. The administration of iron in large doses by mouth before, in the course of and after malarial therapy attenuates the anemia. Sixty paralytic patients had malarial treatment with this strain of Plasmodium malariae. Four patients died.

AUSTRALIA

(From Our Regular Correspondent)

Jan. 17, 1942.

The White Man in the Tropics

The problem of colonization assumes every year a greater importance to Australia. What many writers fail to realize is that conditions in the Australian tropics are widely different from those in territories climatically similar and that in consequence the problems must be solved locally and with little help from experiences in other lands. In all other tropical countries there is a large native population acting as a permanent reservoir of endemic disease and, further, the white man is manager and the white woman is supplied with abundant and cheap colored labor in her home. In Australia north of Capricorn the native population is sparse, endemic diseases have little menace and the whole work of the community is carried out by the white race, manual as well as administrative, unskilled as well as technical. A vast amount of research work has been undertaken in an attempt to disentangle the effects of tropical diseases from the effects of climate. It has also only recently been appreciated that malnutrition plays a much more important part than was previously realized. The shortage of milk and many protective vegetables cannot fail to lower vitality. The most recent contribution to this vexing problem of man in the tropics comes from the Medical School of the University of Queensland. Prof. Douglas Lee in his brochure "A Basis for the Study of Man's Reaction to Tropical Climates" has built up from the various sources available an ordered and concise picture of the way in which the human body reacts to the heat elements in climate. The bulk of the actual material comes from the existing literature, but original research is frequently introduced. Starting from simple physical concepts, the bodily activities have been examined, first singly or in simple groups and then in greater complexity. This is followed by considerations of the body as a whole. Finally the immediate practical applications and significance of the prior studies are discussed with a view to linking the more "academic" and fundamental considerations to the everyday problems with which they are trying to cope. We need still more facts, but Professor Lee has coordinated what facts we have into a more useful and rational conception than has previously existed.

Hydatid Disease in New Zealand

Although figures showing the proportion of hydatid cases to the total number of admissions in public hospitals does show some evidence of comparative diminution, it is clear also that the total number of hydatid cases in New Zealand is slightly increasing. These observations are made by Sir Louis Barnett in his annual report in the *New Zealand Medical Journal* regarding the incidence of hydatid disease in New Zealand. There is little or no indication of improvement in the tallies of infected sheep and cattle. Undoubtedly it takes a matter of years to get results in hydatid prevention and eradication, but there is a growing conviction that success will never be achieved without legal enforcement of the precautions recommended. While many dog owners do pay heed to the recommendations embodied in the large output of educational material, the unpleasant fact stands out that far more of them do not. In particular they allow dogs to feed on raw offal and they neglect or refuse to dose their dogs with the tapeworm medicine supplied to them. A study of the data justifies the following deductions: 1. About 120 new cases of hydatid disease are treated in New Zealand every year. About 16 of them are fatal. 2. Roughly half of New Zealand's sheep and cattle have livers and lungs infected with hydatid or tenuicollis cysts. 3. A third or more of country dogs harbor the adult parasite Taenia echinococcus. 4. The South Island, though only half as populous as the North Island, yet has almost as many cases of hydatid disease. This disproportion is largely due to a particularly heavy infestation in the Canterbury district.

Trachoma Among the New Zealand Maori

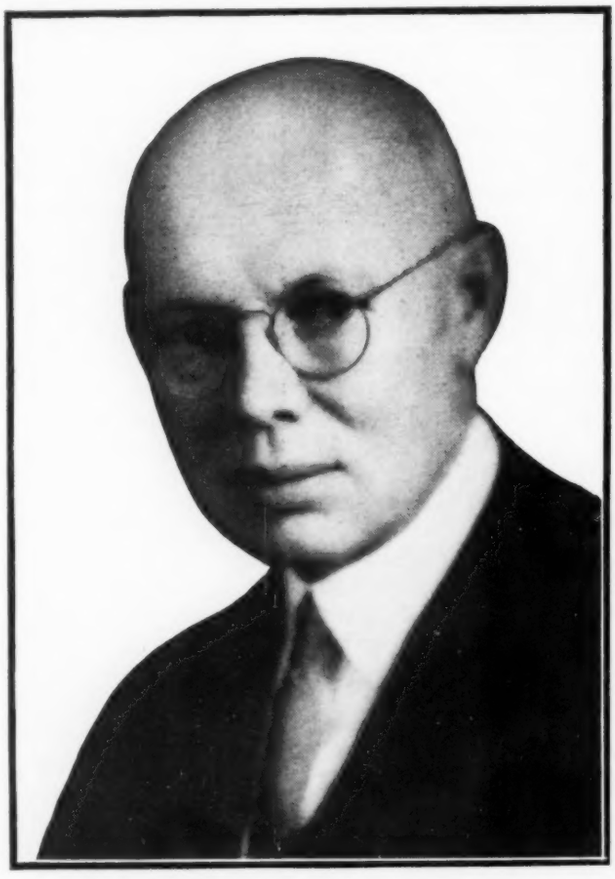
The widespread nature of trachoma in New Zealand is not generally realized. There have even been differences of opinion as to whether real trachoma does exist among the Maoris. Swanston, from the Medical School, Otago, has pointed out that trachoma is not only prevalent but also a cause of needless suffering, occasional blindness and great economic loss.

There are several reasons for this lack of realization of the true state of affairs, not the least of which is the apathy of the Maoris themselves. When a Maori becomes infected he takes little notice until his sight is impaired. But perhaps the most important factor is the remoteness of the majority of the Maori population from centers where they can obtain diagnosis and treatment. District nurses take care of most of the medical needs of the Maoris, and if they recognize trachoma at all they treat it simply with drops and ointment. Generally the disease passes undiagnosed and cases are taken with other cases of conjunctivitis, so that medical practitioners never come to hear of them and they are certainly not notified to the health department. Even diagnosed cases are often treated by district nurses without reference to a medical man and without regard to the accepted practice in the treatment of trachoma, namely the vigorous application of a solid copper sulfate stick to the cocainized lid.

Diagnosis was not attempted in the native schools until this year. Up to one in ten of native children examined were found to be suffering from eye disease. The fact that in a mixed community it is the Maori who becomes infected is perhaps not surprising in view of the unhygienic mode of life of the native race. But it also raises another point, namely racial susceptibility. The origin of trachoma in New Zealand and whether it was introduced by the white man or was already present as a heritage from the far off Eastern derivation of the native race will perhaps never be conclusively settled. It is difficult to discover reference to ophthalmia in Maori legend; but, even if trachoma had been present, reference to it would not be sufficiently specific for it to be recognizable. Nevertheless, with the necessary determination, trachoma could be eliminated in New Zealand within the space of five years. Two things are necessary for an organized attack: a small group of specially trained personnel and the establishment of special clinics. Diagnosis and treatment would be accompanied by adequate education among the Maoris, emphasizing the seriousness of the disease.

Deaths

Charles Alfred Dukes ✠ Oakland, Calif.; Vice President of the American Medical Association, died on March 13 at a local hospital as the result of an intestinal infection, aged 69. Dr. Dukes was born in Numa, Iowa, April 23, 1872, and graduated from the Cooper Medical College, San Francisco, in 1895. For many years he was a visiting surgeon at the Veterans Administration Facility at Livermore, Calif., and he was also a member of the staffs of the Merritt Hospital, the Highland-Alameda County Hospital in Oakland, and the Fairmont Hospital in San Leandro. Throughout his career Dr. Dukes gave freely of himself to public service and to medical organization. In the California State Medical Association he had occupied practically all offices, including that of president. He had been chairman of the Cancer Commission and of the Public Relations Committee. In 1941 he was made a member of the Alameda County Institutions Commission, and in 1942 he was appointed a director of the California Safety Council. In the American Medical Association he had served previously as a member of the House of Delegates from 1933 to 1938 and in 1940. In 1940 he became a member of the Committee on Medical Preparedness and more recently had been made chairman of the Corps Area Committee of the Procurement and Assignment Service for Physicians, Dentists and Veterinarians. He was a member of the American College of Chest Physicians and also a fellow of the American College of Surgeons, of which he was formerly vice president. In every phase of medical activity in California his wise judgment and leadership had been highly prized and in recent years equally in all phases of national concern. Especially in the work of preparedness and of medical service in the war he had given unstintedly of his time, traveling repeatedly from the west coast to Chicago and to Washington to participate in essential conferences.



CHARLES ALFRED DUKES, M.D., 1872-1942

Casey Albert Wood ✠ Pasadena, Calif., professor of ophthalmology emeritus at the University of Illinois College of Medicine, Chicago, died, January 26, at the Scripps Metabolic Clinic in La Jolla eight weeks after a cerebral hemorrhage, aged 85. Dr. Wood was born in Wellington, Ont., Canada, on Nov. 21, 1856. He was educated in private schools and was graduated from the Ottawa Collegiate Institute in 1874. After graduation from the University of Bishop College of Medicine, Montreal in 1877, he practiced in Montreal and was professor of chemistry and pathology at Bishop College from 1878 to 1885. His early training in ophthalmology was taken at the New York Eye and Ear Infirmary and the New York Post-Graduate Medical School in 1886. Courses at many European clinics followed, and in the years 1888 and 1889 he served as assistant surgeon in several London clinics. In 1890 he located in Chicago, where he served as attending ophthalmic surgeon on the staffs at Alexian Brothers', Passavant Memorial and St. Luke's hospitals. He served as professor of ophthalmology on the faculties of Chicago Post-Graduate Medical School, College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois and Northwestern University Medical School. Dr. Wood retired from practice in 1917. In that year he was commissioned a major in the U. S. Army and was assigned to Camp Sherman, Ohio, where he was placed in charge of the eye department at the camp hospital. Later he was made lieutenant colonel on the Surgeon General's staff in Washington, D. C., where he worked on the history of World War I. He retired with the rank of colonel in the Medical Reserve, United States Army. During 1898 and 1899 he was chairman of the Section on Ophthalmology of the American Medical Association and in 1904 a member of the House of Delegates. He served as president of the American Academy of Ophthalmology and Otolaryngology and of the Chicago Ophthalmological Society. He was a member of the Illinois State Medical Society, founding fellow of the American College of Surgeons and of the Institute of Medicine of Chicago. From 1894 to 1901 he served as editor in chief of the *Annals of Ophthalmology*, and from 1902 to 1908 he held the same position on the *Ophthalmic Record*. The latter journal was merged with others to form the *American Journal of Ophthalmology*, and he served the new publication as editor in chief from 1908 to 1914. He published many articles in his special field as well as many translations of treatises on the eye. He was the author of "A System of Ophthalmic Therapeutics," "A System of Ophthalmic Operations" and "The American Encyclopedia of Ophthalmology." He was the coauthor with T. A. Woodruff of "Commoner Diseases of the Eye." After World War I Dr. Wood spent two years in British Guiana studying the eyes of birds and reptiles. During the succeeding years he pursued his studies in various countries of the Far East. Thereafter until two years ago he resided in Rome, Italy, and continued the translation of foreign language works on ophthalmology. His collection of books on ornithology and his medical library, together with rare books on ophthalmology collected during his travels, were given to McGill University, Montreal, Que., Canada, where he received the honorary doctor of medicine in 1906 and the doctor of laws in 1921.

Henry Dawson Furniss ✠ New York; University of Virginia Department of Medicine, Charlottesville, 1899; in 1913 member of the House of Delegates of the American Medical Association; professor of obstetrics and gynecology at the New York Medical College; formerly professor of gynecology at the New York Post-Graduate Medical School, Columbia University; member of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons, Southern Surgical Association and the American Urological Association; fellow of the American College of Surgeons; attending obstetrician and gynecologist, Flower and Fifth Avenue hospitals; visiting surgeon, Metropolitan Hospital; consulting gynecologist, New York Post-Graduate Hospital, Broad Street Hospital, New Rochelle (N. Y.) Hospital, St. Luke's Hospital, Newburgh, N. Y., Holy Name Hospital, Teaneck, N. J., Hackensack (N. J.) Hospital and the All Soul's Memorial Hospital, Morristown, N. J.; consulting cystoscopist, New York Infirmary for Women and Children; served during the World War; aged 63; died, January 25, of coronary occlusion.

Herbert Fox ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1901; professor of comparative pathology at his alma mater since 1927; member of the American Association of Pathologists and Bacteriologists, American Philosophical Society, American Society of Clinical Pathologists and the College of Physicians of Philadelphia; chief of the state department of health laboratories from 1906 to 1911; pathologist, Rush Hospital for Consumption and Allied Diseases; pathologist, Children's Hospital, from 1915 to 1926; pathologist, Philadelphia Zoological Society; served as chief of the cantonment laboratory at Camp Zachary Taylor, Louis-

ville, Ky., during the World War; director of the William Pepper Laboratory of Clinical Medicine at the Hospital of the University of Pennsylvania; author of "Elementary Bacteriology and Protozoology" and "Disease in Captive Wild Mammals and Birds"; co-author with Dr. Alfred Stengel of the eighth edition of "Textbook of Pathology"; aged 61; died, February 27, of coronary thrombosis.

Claud R. G. Forrester ✠ Chicago; Bennett Medical College, Chicago, 1902; formerly professor of osteology at his alma mater, which is now known as Loyola University School of Medicine, where he was clinical professor of surgery; fellow of the American College of Surgeons; for three years a member of the Illinois Naval Reserve, and during the World War served as major with the British Army; on the attending surgical staff of the Chicago Memorial and Edgewater hospitals and on the attending staff of St. Joseph Hospital; aged 61; died, February 27, at his farm in Garden, Mich.

Robert Livingston Loughran, Sharon, Conn.; Columbia University College of Physicians and Surgeons, New York, 1899; at one time professor of otolaryngology at the New York Post-Graduate Medical School; served during the World War; member and formerly secretary of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; formerly on the staffs of Lying-in Hospital and the New York Post-Graduate Hospital, New York; aged 68; died, January 27, of coronary thrombosis.

Max William Jacobs ✠ St. Louis; Washington University School of Medicine, 1905; assistant professor of clinical ophthalmology at his alma mater; past president of St. Louis Ophthalmic Society; member of the American Academy of Ophthalmology and Otolaryngology; assistant ophthalmologist, Barnes, St. Louis Children's and St. Louis Maternity hospitals; on the staff of the Jewish Hospital; aged 62; died, January 9, of coronary thrombosis.

Clinton Austin Kane, Elkton, Md.; Jefferson Medical College of Philadelphia, 1903; member of the Medical and Chirurgical Faculty of Maryland; county health officer; formerly member of the state board of health of Virginia; served during the World War; aged 61; died, Dec. 27, 1941, at Perryville, of carcinoma of the bladder.

Walter Whitman Hendee ✠ North Vassalboro, Maine; College of Physicians and Surgeons, Boston, 1914; served during the World War; formerly member of the school board; aged 52; died, January 13, in the Veterans Administration Facility, Togus, of adenocarcinoma of the liver, lung, pleura and ribs.

Charles Edward Sceleth ✠ Chicago; Rush Medical College, Chicago, 1896; served during the World War; formerly medical superintendent of the House of Correction and Sceleth Emergency Hospital; aged 68; died, January 19, in the Albert Merritt Billings Hospital of bronchogenic carcinoma.

Luther Bayne Holmes, Moorefield, Ky.; Louisville and Hospital Medical College, 1908; member of the Kentucky State Medical Association; aged 57; died, January 25, in the Good Samaritan Hospital, Lexington, of pneumonia following a cholecystostomy.

Chester Horton Longacre, Lincoln, Neb.; University of Louisville (Ky.) Medical Department, 1908; member of the Nebraska State Medical Association; aged 58; died, Dec. 8, 1941 in the Clarkson Memorial Hospital, Omaha, of pulmonary embolism.

Bush McLaughlin, Dalzell, S. C.; University of Virginia Department of Medicine, Charlottesville, Va., 1890; University of Maryland School of Medicine, Baltimore, 1891; aged 75; died, Dec. 20, 1941, of injuries received in an automobile accident.

Peter Thomas Geyerman, Hot Springs, S. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; member of the South Dakota State Medical Association; aged 67; died, January 3, of cerebral hemorrhage.

Ranney Yale Lyman, Chicago; Northwestern University Medical School, Chicago, 1940; Elizabeth J. Ward fellow in radiology at his alma mater; aged 33; died, Dec. 22, 1941, at his home in Helena, Mont., of chronic hepatitis.

Herbert Alonzo Copsey ✠ Alliance, Neb.; Lincoln Medical College of Cotner University, 1906; fellow of the American College of Surgeons; on the staff of St. Joseph's Hospital; aged 61; died, January 14, of heart disease.

Wade Hampton Bynum, Germanton, N. C.; University College of Medicine, Richmond, Va., 1900; member of the Medical Society of North Carolina; aged 82; died, January 10, of heart disease.

C. D. D. M. M. S. Langrall, Arcadia, Neb.; Ensworth Medical College, St. Joseph, Mo., 1901; member of the Nebraska State Medical Association; aged 66; died, Dec. 26, 1941.

Woodburne Roszel Avis, New Haven, Conn.; College of Physicians and Surgeons, Baltimore, 1894; aged 75; died, Nov. 16, 1941, of cerebral hemorrhage and arteriosclerosis.

Frank West Coile, Winterville, Ga.; Atlanta Medical College, 1891; member of the Medical Association of Georgia; aged 77; died, Dec. 14, 1941, of coronary occlusion.

James Anderson Burks, Benton, Ark.; College of Physicians and Surgeons, Little Rock, 1910; member of the Arkansas Medical Society; aged 66; died, Dec. 20, 1941.

Patrick John Rowan, Pittsburgh; College of Physicians and Surgeons, Baltimore, 1885; aged 81; died, Nov. 19, 1941, of coronary thrombosis and arteriosclerosis.

Albert Stanley Freedman, Scranton, Pa.; University and Bellevue Hospital Medical College, New York, 1907; aged 58; died, Nov. 15, 1941, of coronary occlusion.

Quinter Olen Gilbert ✠ Oakland, Calif.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1914; aged 58; died, Dec. 3, 1941.

Rikita Honda, Los Angeles; Chiba University of Medicine, Japan, 1918; member of the California Medical Association; aged 48; died, Dec. 14, 1941.

Frank W. Vance, Memphis, Tenn.; Memphis Hospital Medical College, 1881; aged 80; died, Nov. 22, 1941 in Bolivar of bronchopneumonia.

William Brady Ritter, Erie, Pa.; Kentucky School of Medicine, Louisville, 1893; aged 79; died, Nov. 27, 1941, of cerebral hemorrhage.

Condie Butler Beck, Rising Sun, Ind.; Kentucky School of Medicine, Louisville, 1893; aged 73; died, January 23, of coronary occlusion.

Frew Albertis Tucker, Iowa City; Hahnemann Medical College and Hospital, Chicago, 1899; aged 72; died, Dec. 20, 1941, of carcinoma.

Paul Zotique Hebert, Los Angeles; McGill University Faculty of Medicine, Montreal, Que., Canada, 1872; aged 92; died, Dec. 3, 1941.

George Northrup Jack ✠ Buffalo; University of Buffalo School of Medicine, 1895; aged 72; died, January 12, of cerebral hemorrhage.

John Joseph Stack, Los Angeles; Harvard Medical School, Boston, 1907; served during the World War; aged 57; died, Nov. 25, 1941.

Thomas H. Conarroe, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1893; aged 69; died, Dec. 18, 1941.

August C. Busch, Cincinnati; Medical College of Ohio, Cincinnati, 1894; chairman of a draft board; aged 70; died, Dec. 28, 1941.

James Douglas MacLean, Edmonton, Alta., Canada; Trinity Medical College, Toronto, Ont., 1900; aged 70; died, Nov. 26, 1941.

William Odell Dyer, Oxford, Wis.; Detroit College of Medicine, 1894; aged 74; died, Nov. 24, 1941, of carcinoma of the stomach.

Tasso O. Felix, Downs, Kan.; Marion-Sims College of Medicine, St. Louis, 1898; aged 80; died, Dec. 12, 1941, in Denver.

Joseph W. Taylor, La Mesa, Calif.; University of Wooster Medical Department, Cleveland, 1872; aged 93; died, Nov. 25, 1941.

Atlas Thompson Hembree, Windor, Calif.; Cooper Medical College, San Francisco, 1905; aged 71; died, Dec. 28, 1941.

John M. H. Blau, Louisville, Ky.; Medical College of Ohio, Cincinnati, 1881; aged 82; died, Nov. 29, 1941.

DIED IN MILITARY SERVICE

Henry Hansford Ward, Miami, Fla.; University of Tennessee College of Medicine, Memphis, 1933; was called to active duty on July 14, 1941, as a first lieutenant in the medical reserve corps of the United States Army; was stationed at the 33d Surgical Hospital, Fort Oglethorpe, Ga.; aged 35; died, January 20, of staphylococcus aureus septicemia.

Correspondence

APPLICATION OF SULFONAMIDE SOLUTIONS TO NOSE

To the Editor:—Dr. Russell Fletcher (THE JOURNAL, Oct. 4, 1941, p. 1204) has cautioned against the local application of sulfonamide drugs on chronically inflamed sinuses. His view is based on his own experience with an unusual case of odontogenous antritis and also on an opinion by Dr. M. L. Tainter, a pharmacologist, who stressed the caustic action of these drugs and ascribed this effect to their alkalinity.

Briefly, Dr. Fletcher's case revealed an extremely foul exudate emanating from a fistulous tract in the mouth. Osteomyelitis in the vicinity of the tooth socket was present with loosening of the adjacent tooth. Frequent irrigations of the usual kind were of no avail and the use of 5 to 10 per cent sodium sulfathiazole in physiologic solution of sodium chloride —according to the procedure of Dr. F. M. Turnbull of Los Angeles—was instituted. However, surgical intervention finally had to be instituted and revealed widespread necrosis. Separation from viable tissue was extremely difficult, but recovery was uneventful.

This record recalled a special series of patients with odontogenic maxillary sinusitis whom I have observed. They never had been treated with any of the sulfonamides. The characteristic features of the group consisted of a primary macroscopic dental focus while the inflammatory process involved either the buccal or the antral mucosa or both. Typically, the primary lesion was a chronic osteomyelitis while the secondary extension—the "acute exacerbation"—was characterized by rapid extension, more especially along the inner than the outer aspect of the bony wall, with eventual final progression to the nasal wall.

It seems to be insufficiently known that thus far no variety of conservative treatment has effected a cure even after eradication of the primary focus but rather that a radical procedure on the antrum with removal of all necrotic tissue is essential and will promptly induce healing.

The instance that Dr. Fletcher reports fits well into this group of cases of odontogenic chronic antritis. In my opinion Dr. Fletcher's case is poorly chosen to decide a question which is of enormous therapeutic importance. The physician is familiar with surgical infections which are said to be favorably influenced by the local application of these drugs. The tolerance of the mucous membranes toward these drugs, furthermore, has not yet been sufficiently studied to contraindicate their use on the basis of 1 case. However, Dr. Fletcher's point should serve as a caution in the evaluation of results of the subsequent investigations in this field; in my opinion the discontinuance of topical drug therapy on the basis of Dr. Fletcher's experience, on the other hand, would be founded on an erroneous conclusion.

WALTER D. KLESTADT, M.D., New York.

NOTE.—The communication was referred to Dr. Fletcher, who replies:

To the Editor:—I am glad to have this comment, which is clear and decidedly to the point. I agree that conclusions should not be far reaching when they are based on 1 case. The reason I recorded my observations in this communication was that I had an unusual sequence of events, and the most likely cause to which I could attribute my results was the fact that I had used the sodium salt of sulfathiazole.

As this commentator states, this is a typical case of a foul infection of the antrum resulting from dental infection and extraction. This is a rather common experience that all ear, nose and throat specialists frequently see, and it is also a common occurrence for exodontists in the dental field. It is common to see necrosis and a large amount of destruction in the antrum in such cases. The unusual part of this particular case was the fact that neither the exodontist, who is a specialist in this field and who has a large practice, nor I had ever seen a case in which the lining membrane of the antrum was so completely charred or destroyed as in this case. It did not seem to be a simple necrosis. The lining of the antrum had been replaced or at least covered by a black substance that looked like clay.

As neither of us had ever seen such a condition, in spite of the fact that both of us have seen many cases of antrum infection following a tooth extraction, I consulted the pharmacologist Dr. Tainter of Stanford University. From him I learned that the sodium salts of all the sulfonamide drugs are extremely alkaline and that the caustic action of this particular solution could have been severe enough to cause the burning or charring of this membrane. Prior to that time I had not realized how caustic the sodium salts of this drug were, and I therefore felt that it was important to warn all physicians who were using the sodium salts of this drug that the drug was highly alkaline (in fact it has a p_H of 10 to 11).

As to whether the sodium salts of this drug or any other medication should be used in such cases I did not try to say. It may be possible that in the future either a strong acid or a strong base such as sodium hydroxide will be used in cases such as these; however, I do know that most physicians with whom I have spoken regarding the drug had no idea how caustic this particular drug was. I felt therefore that they should be warned accordingly. If a physician wishes to use 10 per cent sodium hydroxide he can do so, but he should realize what the reactions will be before doing so.

RUSSELL FLETCHER, M.D., San Francisco.

THE CAUSE OF CHRONIC NEPHRITIS

To the Editor:—In reading the paper on "Treatment of Acute Nephritis" by Drs. Francis D. Murphy and Bruno J. Peters (THE JOURNAL, January 17) we were surprised that mention was not made, in discussing the etiology, diagnosis, treatment and prognosis, of obstructing lesions in the ureter, at the vesical neck or in the urethra.

It is difficult for a urologist to understand how it could be that some of the 205 patients in their study did not have an obstructing lesion which played a part in making the kidney vulnerable for the toxic agent that brought on the acute glomerular nephritis.

Drs. Murphy and Peters say "Why some patients who have recovered from acute nephritis are completely healed and others progress gradually into the stage of chronic nephritis is an unsolved problem." Might not an obstructing lesion be at least one of the factors which caused 43 per cent of their patients to have a persisting "latent or chronic nephritis"?

Hydronephrosis, slight or considerable in extent, may be present without pain or symptoms directing attention to the existence of this condition.

Might not an obstruction be the reason that "the prognosis was found to be no better when the initial stage was mild than when it was severe or stormy"?

EDGAR G. BALLENGER, M.D.
HAROLD P. MCDONALD, M.D.
Atlanta, Ga.

NOTE.—This communication was referred to Dr. Murphy, who replies:

To the Editor:—Obviously our confession of lack of exact information concerning the factors which may influence chronicity leaves us in no position to reject a practical suggestion. However, before we accept the view that obstructive lesions play an important role in retarding the healing of nephritis, as

mentioned in the communication, it would seem necessary not only to observe such lesions in a series of cases of unhealed nephritis but to show that such lesions impaired healing. We are not aware of this kind of a study. In too few of our cases to settle the point in question urologic investigations were made and no obstructive lesions were found. It is not contended that they were searched for, but since the work was done by competent urologists we do not believe that significant lesions were overlooked.

Since obstructive lesions are not infrequently found in pyelonephritis, their presence would bring to mind the difficulty that is sometimes encountered in differentiating pyelonephritis from glomerulonephritis. This does not mean that obstructive lesions may not play a part in glomerulonephritis, but if they do their presence and importance have not been duly emphasized.

FRANCIS D. MURPHY, M.D., Milwaukee.

METRIC VS. ENGLISH MEASUREMENTS

To the Editor:—The following sentence is from a recent article appearing in the proceedings of one of our large clinics: "During the 200 mile (322 kilometer) drive he became steadily worse and by noon somewhat stuporous." The conversion of miles into kilometers seems to me to be quite unnecessary and, in fact, annoying. It does bring up the subject, somewhat indirectly, of the use of the metric and other systems in medical practice and the report of cases.

Like a great many physicians, I approve of the metric system in prescription writing, although I rarely use it. I suggest that in the printing of prescription blanks there be printed in the lower left hand corner a table such as the following:

Grains	Gm. or Cc.
1/150	0.0004
1/120	0.0005
1/100	0.0006
1/6	0.011
1/4	0.016
1	0.065
15	1.0
60 (1 drachm)	4.0
1 oz.	32.0

By forcing ourselves to convert the apothecary measure into the metric equivalent no doubt within a reasonable time we would be able to write the metric system without first thinking of its equivalent. And certainly the reading of modern medical articles would be easier.

In short measurements such as those of chest and heart widths and proctoscopic distances centimeters appeal to me more than inches, but for a person's height I must use feet and inches. Likewise I prefer pounds to kilograms. Here too a change in thinking could be effected. Manufacturers should be asked to provide medical scales with both pound and kilogram markers, and height indicators with centimeters as well as inches. In the meanwhile, a home made conversion table for kilograms and centimeters could be put on the wall or attached to the scales.

Further on in the article that I was reading occurred the expression "2½ ounces (74 cc.)." This conversion could be omitted, since in liquid measurements (excepting prescriptions) most physicians have become quite conversant with cubic centimeters. In fact it is more natural to say 300 cc. of blood than 10 ounces. This is one part of the metric system, thanks to syringes and ampules, which we seem to have mastered. There are, of course, some physicians who are quite well versed in ounces, quarts and even fifths of gallons.

When it comes to clinical thermometers, I can see no advantage of the Centigrade over the Fahrenheit. To me it is almost as annoying to be told that 102 F. is so and so C. as to be told that 200 miles equal 322 kilometers.

ALAN R. ANDERSON, M.D., Freeport, L. I., N. Y.

VITAMIN K FOR THE NEWBORN

To the Editor:—In a recent issue of THE JOURNAL (February 28, p. 697) Dr. Sanford and his associates published an article with the important title "Is Administration of Vitamin K to the Newborn of Clinical Value?" One looks in vain, however, for a straightforward answer to this question in their paper. From their emphasis that hemorrhagic manifestations in their series were as frequent in the infants treated with vitamin K as in the untreated controls, it may be surmised that they are doubtful concerning the efficacy of vitamin K in the prevention of the hemorrhagic disease of the newborn.

The question that these authors have raised deserves serious consideration, since it involves the potential safety of many newborn babies. I feel that enough clinical results have been reported to answer the question unequivocally and emphatically in the affirmative.

There is obviously still some misunderstanding as to what constitutes hemorrhagic disease of the newborn. The condition may be defined as a clinical entity, occurring during the first week of life, which is usually self limited but may be fatal. It is recognized by external and internal bleeding and by an exceedingly low prothrombin content of the blood, which is promptly restored to normal through vitamin K. Not all bleeding observed in young infants is, however, due to hypoprothrombinemia. Unfortunately the hemorrhagic diseases are still plagued by the widely accepted fallacy that the coagulation of blood is synonymous with hemostasis. It is necessary to emphasize that the vascular contractive response to injury is equally, if not even more, important in the protective reaction against hemorrhage. Likewise, clot retraction, platelet agglutination and other factors play a part in this defense mechanism. Thus babies born of mothers with thrombopenic purpura may show a transient purpuric type of bleeding.

There can be no doubt that many cases of serious or uncontrolled hemorrhage can be traced to injury of large vessels which may be so extensive that the hemostatic defense, even though normal, is unable to cope with the bleeding. Thus, in 4 cases reported by Dr. Sanford and his associates in which death from cerebral hemorrhage occurred, tentorial tears were found. The delicate blood vessels of the baby are easily injured and massive hemorrhage immediately occurs.

The facts just enumerated do not invalidate the importance of the hypoprothrombinemic bleeding of the newborn. Diminution of plasma prothrombin as a cause of bleeding is no longer questioned. Drs. Bancroft, Stanley-Brown and I, as early as 1934, reported that the bleeding in jaundice was due to a low prothrombin level, and in 1936 I demonstrated that, when the prothrombin in chicks and rabbits was reduced to a certain level, spontaneous hemorrhages occurred. All now agree that the prothrombin of most infants not treated with vitamin K drops (sometimes to low levels) during the first week. It is logical to suspect that this hypoprothrombinemia should lead to hemorrhage, and this is supported by the fact that the time of the highest incidence of hemorrhage coincides with the period of low prothrombin level.

Most convincing, however, are the actual recorded cases in which a low prothrombin level was found and the bleeding promptly stopped after the administration of vitamin K. I have seen 1 case in which practically the whole scalp was lifted by an extensive hematoma and there was active bleeding from a forceps cut. Administration of vitamin K promptly stopped the hemorrhage, and a complete recovery resulted. Recently I have seen an infant 3 months old suffering from malnutrition and gastroenteritis, who began passing blood in the stools. The prothrombin level was found to be 6 per cent. Synthetic vitamin K intravenously promptly stopped the hem-

orrhage and elevated the prothrombin level. In the face of such evidence, one must conclude that prothrombin deficiency, whether it occurs in babies or in adults, brings about a hemorrhagic tendency and that the hypoprothrombinemic period following shortly after birth is potentially dangerous.

In regard to cerebral bleeding, it is clear that vitamin K will have little or no effect if the tentorium is torn or a large cerebral or meningeal artery is severed. This type of cerebral bleeding manifests itself soon after birth, but there is a second form which appears in babies who are normal for several days before signs of intracranial bleeding are noted and who at autopsy show no serious injury of any large blood vessel. It is the latter form that one hopes will be benefited or prevented by vitamin K. It is well to remember, however, that vitamin K will never be a substitute for obstetric skill and gentleness in manipulation and handling of the newborn.

If the aim of Dr. Sanford and his associates in presenting their paper is to emphasize that hemorrhages in the newborn can occur from causes other than prothrombin deficiency, they are serving a laudable purpose; but, on the other hand, if they are attempting to depreciate the value of vitamin K in preventing and curing the hemorrhagic disease of the newborn one is forced for the sake of the newborn baby to take sharp issue with them.

ARMAND J. QUICK, M.D.
Marquette University School of Medicine, Milwaukee.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

UNITED STATES PUBLIC HEALTH SERVICE

Examination. Assistant Surgeon (medical only), commissioned corps. Examinations will be held as follows:

U. S. P. H. S. Hospital, Fort Worth, Texas.....March 27
U. S. Marine Hospital, New Orleans.....March 30
Liaison Office, U. S. P. H. S., Room 319, Grant Bldg., Atlanta, Ga. .....March 31

Apply Surgeon General, U. S. P. H. S., Washington, D. C.

BOARDS OF MEDICAL EXAMINERS

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, March 14, page 918.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* Various centers, June 22-24. *Part III.* Various centers, June. Exec. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Oral. Groups A and B.* Cleveland, Jan. 14-15, 1943. Final date for filing application is Dec. 7. *Written.* Various centers, Nov. 16. Final date for filing application is Oct. 5. Sec., Dr. C. Guy Lane, 416 Marlboro St., Boston.

AMERICAN BOARD OF INTERNAL MEDICINE: *Oral.* St. Paul, April, in advance of the meeting of the American College of Physicians and Philadelphia, June, in advance of the meeting of the American Medical Association. Application should be on file 6 weeks in advance of the date of oral examination. *Written.* Oct. 19. Final date for filing application is Sept. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: *Oral.* New York, May 12-13. Sec., Dr. R. Glen Spurling, 404 Brown Bldg., Louisville, Ky.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral.* Baltimore, June 6 and Philadelphia, June 8. Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Oral and Written.* Chicago, Jan. 9-10. Final date for filing application is Nov. 1. Sec., Dr. Guy A. Caldwell, 3503 Prytania St., New Orleans.

AMERICAN BOARD OF PEDIATRICS: *Written.* Locally, Sept. 18. *Oral.* Chicago, Nov. 2-3. Final date for filing application is July 1. Sec., Dr. C. A. Aldrich, 707 Fullerton Ave., Chicago.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December. Final date for filing application is Oct. 1. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: *Oral. All Groups.* Atlantic City, June 4. Final date for filing application is April 1. Sec., Dr. Byrl R. Kirklin, 102-110 Second Ave., S. W., Rochester, Minn.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Liability of Physicians of Health Foundation.—The defendant National Health Foundation was a voluntary association which contracted with its members to furnish certain medical services, for which the members paid a monthly premium to the foundation. The trustee of the foundation was authorized to employ a medical director who, with such assistants as he might designate, was to furnish all the medical services contracted for by the foundation. The defendant, Dr. Eugene Carbaugh, was appointed medical director, and the defendants, Dr. Glenn C. Carbaugh and Dr. J. Earle Donaldson, were designated as his assistants. The three physicians, the foundation and the trustee occupied the same office space and their respective telephone numbers were identical. A member desiring medical attention would call that number. If no specific physician was requested the trustee would assign any one of the three to the member. The plaintiff was a member in good standing of the foundation from Jan. 8, 1938, to Feb. 15, 1938. Subsequently she sued the three physicians, the foundation and the trustee for damages alleged to have been caused by the defendants' joint and several negligence. From a judgment for the plaintiff, the defendants appealed to the Kansas City court of appeals, Missouri.

When the plaintiff went to the offices of the foundation on Jan. 8, 1938, she requested the services of Dr. Glenn Carbaugh. She complained of general lassitude and of soreness in the wrists. He found her throat irritated, prescribed medicine for her to take and recommended that she have her tonsils out within a few weeks. She returned to her home, went to bed and followed the physician's instructions. The soreness in her wrists increased, however, and spread to her shoulders, through her body and down to her feet. Her limbs swelled conspicuously and she continued to have a temperature and to remain drowsy and "dopey." At times the pain was so severe that she became almost hysterical. On January 12 the physician was called and he visited her at her home. He told her to continue taking the medicine that he had prescribed and said that she would just have to wear the disease out. The swelling became more pronounced and black blotches began to appear on her body and limbs. She could not bear the weight of bedclothes. After numerous calls to the foundation, Dr. Donaldson finally visited the plaintiff on the 20th. He made no examination of the plaintiff but merely asked her how she felt and prescribed more medicine for her to take. Two days later, Dr. Eugene Carbaugh visited the plaintiff in response to a telephone call by the plaintiff's husband, who described the plaintiff's condition in detail. This physician also told the plaintiff to continue taking the same treatment. Quoting from the decision:

> Her condition grew progressively worse until the 29th, when she was unable to feed herself. Her arms and legs were immobile except when moved by some other person. Her pain was such that she cried. It took her fifteen minutes to be taken a few feet to the bathroom. The black blotches had increased in number and size. Her limbs and arms were swollen greatly. She could eat but little. She was in a drowsy semicoma almost all of the time. In the meantime none of defendant's doctors had called nor had plaintiff been advised at any time by any of them that they would not call, nor that they had quit the case. Neither had the foundation called or sent any other doctor, or offered so to do.

It was then that the plaintiff's husband requested Dr. Laurenzana, a physician not associated with the foundation, to take charge of the case. Dr. Laurenzana examined the patient carefully, caused a blood count to be made and took a throat smear for microscopic examination. His diagnosis was hemolytic streptococcus infection caused by a throat infection, and he prescribed sulfanilamide and a light ray treatment. Within five days the plaintiff responded to the treatment and eventually virtually recovered.

At the trial Dr. Laurenzana, called as a witness by the plaintiff, testified that, judging from plaintiff's condition on Jan-

uary 29, a proper examination should have caused a suspicion of the existence of the streptococcic infection as early as January 8 and should certainly have confirmed that suspicion by the 19th. He also stated that if the plaintiff's true condition had been discovered at the outset, and the proper sulfanilamide treatment administered, she would not have gotten into the serious condition in which he found her on January 29 and would have had a complete recovery much sooner than she did. In conclusion, he stated that a person with the symptoms that the plaintiff exhibited should have been under daily observation so that an early diagnosis could have been reached and proper treatment given.

The defendants contended, among other things, that each of the defendant physicians exercised his own independent judgment and that therefore one was not liable for any errors of the others. The court held, however, that the evidence showed the existence of a joint and common enterprise. The physicians were working for a common employer and for a common purpose, they were associated in the same office and each had knowledge of what the others had done or were doing. The defendants also urged that the foundation was not liable for any negligence of the individual defendants. The court pointed out that the plaintiff had relied on her contract with the foundation and, when she became dangerously ill, the foundation's agents not only failed to perform the contract properly but eventually completely abandoned it. Furthermore, the resulting damage to the plaintiff was readily foreseeable. Hence the court held that the negligence of the medical director and his assistants was chargeable to the foundation.

As to the liability of the individual defendants, the court ruled separately regarding each. The law requires every physician, said the court, to possess adequate skill and care for the practice of his profession. The plaintiff did not argue that the defendants failed to possess that degree of efficiency necessary but contended that the defendants were negligent in failing to apply it. The court held that the evidence fully sustained that contention. Dr. Glenn Carbaugh, said the court, was negligent in assuming the care of the plaintiff and then completely abandoning her when she was in a critical condition. Dr. Donaldson, having assumed the care of the plaintiff, was negligent in failing to make an adequate examination and in blindly adopting the erroneous diagnosis of Dr. Glenn Carbaugh when the plaintiff's serious condition was clearly visible to any one; and he, too, was liable for abandoning the case. Dr. Eugene Carbaugh was liable for adopting a wrong diagnosis by another physician, for making no adequate examination on his own behalf and for withdrawing from the case without notifying the plaintiff. In conclusion, the court held that the negligence of the defendant physicians was concurrent and that the defendant physicians were therefore jointly and severally liable for the plaintiff's damages. Judgment for the plaintiff against all the defendants was accordingly affirmed.—*Baird v. National Health Foundation, 144 S. W. (2d) 850 (Mo., 1940).*

Pharmacists: Liability for Error in Compounding Prescription.—In an action for damages against the defendant, Marvin Drug Company, the plaintiffs, husband and wife, alleged that Mrs. Smith was a "free bleeder" and was under the treatment of her private physician. As a part of such treatment, her physician gave her a certain prescription which the defendant compounded. The plaintiffs' complaint alleged in the alternative (1) that the defendant contracted to compound the prescription given to it but that it breached such contract by compounding and delivering to the plaintiff some other and different medicine, the use of which resulted in an aggravation of the illness, and damages, or (2) that the defendant negligently failed and refused to compound and fill the prescription but delivered another and different medicine, and that such negligence caused an aggravation of the plaintiff wife's illness. The court of civil appeals of Texas held that the complaint stated a good cause of action and concluded that the trial court erred in dismissing the suit. Accordingly the judgment for the defendant was reversed and the cause remanded for a trial on the merits. —*Smith v. Marvin Drug Co., 150 S. W. (2d) 875 (Texas, 1941).*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Montgomery, Apr. 21-23. Dr. D. L. Cannon, 519 Dexter Avenue, Montgomery, Secretary.

American Association for Thoracic Surgery, St. Louis, May 13-16. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Anatomists, New York, April 1-3. Dr. Eliot R. Clark, Dept. of Anatomy, University of Pennsylvania School of Medicine, Philadelphia, Secretary.

American Association of Industrial Physicians and Surgeons, Cincinnati, Apr. 13-17. Dr. Edward C. Holmblad, 28 East Jackson Blvd., Chicago, Managing Director.

American Association of Pathologists and Bacteriologists, St. Louis, April 2-3. Dr. Howard T. Karsner, 2085 Adelbert Rd., Cleveland, Secretary.

American Association of the History of Medicine, Atlantic City, N. J., May 3-5. Dr. Henry E. Sigerist, 1900 East Monument St., Baltimore, Secretary.

American Association on Mental Deficiency, Boston, May 13-16. Dr. Neil A. Dayton, 100 Nashua St., Boston, Secretary.

American College of Physicians, St. Paul, Apr. 20-24. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Federation for Clinical Research, Minneapolis, Apr. 20-21. Dr. Thomas M. Durant, 3401 North Broad St., Philadelphia, Secretary.

American Pediatric Society, Sky Top, Pa., Apr. 30-May 2. Dr. Hugh McCulloch, 325 North Euclid Ave., St. Louis, Secretary.

American Physiological Society, Boston, March 30-April 4. Dr. Carl J. Wiggers, 2109 Adelbert Rd., Cleveland, Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 4. Dr. Eugene M. Landis, University of Virginia Hospital, Charlottesville, Va., Secretary.

American Society for Experimental Pathology, Boston, April 1-3. Dr. Harry P. Smith, Medical Laboratory Bldg., Iowa City, Secretary.

American Society for Pharmacology and Experimental Therapeutics, Boston, March 31-April 4. Dr. Raymond N. Bieter, University of Minnesota Medical School, Minneapolis, Secretary.

American Society of Biological Chemists, Boston, Apr. 7. Dr. A. K. Balls, Bureau of Agricultural and Engineering Chemistry, Washington, D. C., Secretary.

American Surgical Association, New Orleans, Apr. 6-8. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

Arkansas Medical Society, Hot Springs National Park, Apr. 27-29. Dr. W. R. Brooksher, 602 Garrison Ave., Fort Smith, Secretary.

Association of American Physicians, Atlantic City, May 5-6. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

California Medical Association, Del Monte, May 4-7. Dr. George H. Kress, 450 Sutter St., San Francisco, Secretary.

Federation of American Societies for Experimental Biology, Boston, March 31-April 4. Dr. D. R. Hooker, 19 West Chase, St., Baltimore, Secretary.

Florida Medical Association, Palm Beach, Apr. 13-15. Dr. Shaler Richardson, 111 West Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Augusta, Apr. 28-May 1. Dr. E. D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Iowa State Medical Society, Des Moines, Apr. 15-17. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

Kansas Medical Society, Wichita, May 11-14. Mr. C. G. Munns, 112 West Sixth St., Topeka, Executive Secretary.

Louisiana State Medical Society, New Orleans, Apr. 27-29. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 28-30. Dr. Richard T. Shackelford, 1211 Cathedral St., Baltimore, Secretary.

Medical Library Association, New Orleans, May 7-9. Miss Anna C. Holt, 25 Shattuck St., Boston, Secretary.

Mississippi State Medical Association, Jackson, May 12-14. Dr. T. M. Dye, P. O. Box 295, Clarksdale, Secretary.

Missouri State Medical Association, Kansas City, Apr. 27-29. Mr. E. H. Bartelsmeyer, 634 North Grand Blvd., St. Louis, Executive Secretary.

National Tuberculosis Association, Philadelphia, May 6-9. Dr. Charles J. Hatfield, 1790 Broadway, New York, Secretary.

Nebraska State Medical Association, Omaha, May 4-7. Dr. R. B. Adams, 416 Federal Securities Bldg., Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 12-13. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, Apr. 21-23. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, New York, Apr. 27-30. Dr. Peter Irving, 292 Madison Ave., New York, Secretary.

North Carolina, Medical Society of the State of, Charlotte, May 11-13. Dr. Roscoe D. McMillan, P. O. Box 232, Red Springs, Secretary.

Ohio State Medical Association, Columbus, Apr. 28-30. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Tulsa, Apr. 29-May 1. Mr. R. H. Graham, 210 Plaza Court Bldg., Oklahoma City, Executive Secretary.

Pacific Coast Oto-Ophthalmological Society, Portland, Ore., May 11-14. Dr. C. Allen Dickey, 450 Sutter St., San Francisco, Secretary.

South Dakota State Medical Association, Sioux Falls, May 13-15. Dr. Clarence E. Sherwood, 107½ Egan Avenue South, Madison, Secretary.

Tennessee State Medical Association, Memphis, Apr. 14-16. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

Texas, State Medical Association of, Houston, May 11-14. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

CENTRAL SOCIETY FOR CLINICAL RESEARCH

Fourteenth Annual Meeting, Held in Chicago, Nov. 7 and 8, 1941

The President, DR. LAWRENCE D. THOMPSON, St. Louis, in the Chair

Congenital Malformations on a Nutritional Basis in Rats

DR. JOSEF WARKANY and ROSE C. NELSON, PH.D., Cincinnati: When female rats are reared and bred on Steenbock and Black's rachitogenic diet number 2956 supplemented with viosterol to forestall the development of rickets, congenital malformations appear in about one third of their offspring. External inspection of the newborn animals reveals some of the congenital malformations, such as shortening of the mandible, protrusion of the tongue and syndactylism of the fingers and toes. The skeletal abnormalities can be studied better after the young are cleared by the Schultze-Dawson method. Then shortening or absence of the tibia, fibula, radius and ulna, shortening of the mandible and fusion of the ribs and of the sternal centers of ossification can be seen in such cleared specimens. Gross abnormalities of the soft tissues can also be observed in a few animals. Microscopic histologic examination of the abnormal skeletal structures reveals delay of ossification, persistence of cartilage in places where ossification should have taken place and abnormalities in the preformed cartilage itself.

The congenital malformations can be prevented by the addition of 2 per cent dried pig liver to the deficient diet of the mother. An alcoholic extract of dried pig liver has been found to be equally protective. The calcium content of the diet also seems to play an important role, since a reduction of the calcium carbonate content of the diet from 3 to 1 per cent results in a significant reduction of the incidence of abnormal offspring.

Abnormal and normal offspring can be obtained alternately from the same female when the deficient diet and the diet supplemented by liver are fed alternately. The experimental results described have been obtained in two different strains of rats. It seems that the normal prenatal bone development of these rats depends on a nutritional factor which is absent or indequate in the deficient diet and present in large amounts in liver.

DISCUSSION

DR. M. J. SHAPIRO, Minneapolis: Did you investigate the heart in these rats? How did the deficient diet affect the size of litters?

DR. JULIAN E. BENJAMIN, Cincinnati: What was the effect on the female, and did it make any difference in the course of gestation when the diets were changed?

DR. JOSEF WARKANY, Cincinnati: The hearts have not yet been examined. The average litter size on the deficient diet is five and two tenths, while that on the stock diet is six and eight tenths. While rats on the stock diet can be bred at an age of 2½ to 3 months the animals on the deficient diet often cannot be bred before they are 6 months old. In the experiment of alternating diets the mother's diet was changed before the next mating. Whenever the mother was changed from the deficient diet to the diet containing liver, the subsequent litter consisted of entirely normal offspring.

Vitamin B Complex Studies in Dogs

DR. PAUL J. FOUTS, Indianapolis: In dogs fed a low protein diet supplemented with thiamine hydrochloride, nicotinic acid, riboflavin, pyridoxine hydrochloride and either pantothenic acid or purified liver extract a deficiency state developed characterized by loss of appetite, substantial loss of weight, moderate to severe anemia and peptic and cutaneous ulcers. The condition was prevented by an increase of protein in the diet or by the addition of crude liver extract to the low protein diet. It was not cured or prevented by the addition of cystine, choline, para-aminobenzoic acid, insoitol or an eluate of clay absorbate of liver extract.

DISCUSSION

DR. C. A. DOAN, Columbus, Ohio: Was there any disturbance of the white cell equilibrium in these dogs?

DR. H. M. SHEAFF, Oak Park, Ill.: Were observations made on the gastric acidity?

DR. PAUL J. FOUTS, Indianapolis: In most of the dogs on a low protein diet there was terminally a high white cell count. That was pretty consistent, and it went up as high as 90,000 in some animals. We did not test the gastric acidity routinely. In a few dogs examined there was a slight decrease in the free acid.

The Influence of Sex Hormones on Natural Resistance

DR. EMMERICH VON HAAM and IRENE ROSENFELD, Columbus, Ohio: Adult male and female mice, after having received varying amounts of chemically pure estrone, progesterone and testosterone, were infected experimentally with a laboratory strain of type I pneumococcus which killed laboratory animals after an average period of twenty-six to thirty-six hours. It was found that the female sex hormone increased the resistance of mice to experimental pneumococcic infection.

In another series of experiments the effect of estrone on the natural and acquired antibodies of castrated and noncastrated rabbits was investigated. Antibody curves showed a definite increase in the specific and nonspecific antibodies in animals receiving large doses of female sex hormone before and during experimental immunization.

DISCUSSION

DR. CARL G. HARFORD, St. Louis: Did you determine how many minimal lethal doses of pneumococci were used in the first experiment?

DR. EMMERICH VON HAAM, Columbus, Ohio: Our bacterial suspension was so standardized that it killed mice within thirty-six hours in a dilution of 1: 100,000.

The Therapeutic Use of a Synthetic Estrogen

DR. EDGAR S. GORDON, Madison, Wis.: Since the effectiveness of diethylstilbestrol as an estrogenic substance for clinical use was established, interest in other possible therapeutic agents of the same type has increased. One such preparation is the methyl ether of diethylstilbestrol, which in animal experiments has proved to be a highly effective estrogenic compound with prolonged action. Since the ether linkage is known to be resistant to rupture under physiologic conditions, this material should release its estrogenic potency slowly over a prolonged period of time. This indeed has been found to be the case, since in rats it has been possible to produce continuous estrus for as long as nine months with one injection.

Clinical trial of this compound (to be referred to as RG-20) has given interesting results. The patients studied were all women with menopausal complaints which had appeared either spontaneously or as a result of roentgen or surgical castration. Criteria of effectiveness have consisted of the patient's own report on the progress or regression of symptoms and that on the vaginal smear according to the technic of Papanicolaou. Fifteen cases have been studied in detail over a period of many months and in 10 others the course has been followed by a much shorter time. Of these, in only 2 cases was it necessary to stop the use of RG-20 completely because of nausea and vomiting. In 3 others these symptoms were slightly troublesome but were tolerated during the short time they appeared after each injection because of the extremely favorable results. One instance of sensitivity, presumably to the sesame oil used as a solvent, was encountered. In all other cases results were completely satisfactory, with periods of control of symptoms up to four weeks following a single injection. RG-20 appears to be an excellent estrogenic preparation for use when prolonged, sustained action is desired.

DISCUSSION

DR. E. PERRY MCCULLAGH, Cleveland: Sometimes when diethylstilbestrol is used for several weeks menorrhagia occurs and is difficult to control if administration of the drug is continued. With such a long-acting material as RG-20 has menorrhagia been encountered?

DR. CYRIL M. MACBRYDE, St. Louis: Was endometrial biopsy done on the patients to see whether or not excessive changes were taking place in the endometrium?

DR. PAUL STARR, Chicago: What was the course of the nausea during the thirty days of symptomatic control after a single injection of 20 mg.?

DR. E. S. GORDON, Madison, Wis.: The intensity of the estrogenic action and the nausea appeared to be greatest during the first twenty-four to forty-eight hours. If nausea did not appear within the first twenty-four hours, it usually did not appear at all. I have not done endometrial biopsies. The menorrhagia I have seen occurred only in a patient with an enlarged uterus. This occurred with the diethylstilbestrol therapy only and not with the RG-20 therapy. On cessation of therapy all evidence of menorrhagia stopped and the uterus went back to normal size, and later the menopausal symptoms came back. They could not be controlled by administration of estrone or estradiol without the production of further vaginal bleeding. That is the only case in which I have seen excessive bleeding.

Changes in Liver, Blood and Bone Marrow Produced by Estrone, Estradiol and Diethylstilbestrol

DRS. CYRIL M. MACBRYDE, DANTE CASTRODALE and ELSON B. HELWIG and OLGA BIERBAUM, B.S., St. Louis: Clinical studies have resulted in a variance of opinion among different groups of investigators regarding the toxicity of diethylstilbestrol. To clarify this question, large estrogenically equivalent doses of estrone, estradiol and diethylstilbestrol were given to dogs. Changes were produced in the liver, blood and bone marrow by each of these estrogens, and these changes were indistinguishable as to quality and degree. In the peripheral blood there is at first leukocytosis and then thrombocytopenia, followed by hemorrhage and anemia. The bone marrow showed first early myeloid hyperplasia, then decrease or disappearance of megakaryocytes and finally diffuse hypoplasia. The hepatic changes consisted of fatty degeneration and hydropic degeneration. They occurred before the appearance of the hemorrhagic state and presumably were the result of direct action on the liver cells. The doses used were much larger than those employed clinically. No suggestion of similar toxic changes has been found in our clinical studies.

DISCUSSION

DR. EMMERICH VON HAAM, Columbus, Ohio: In our experiments on diethylstilbestrol my associate and I used estrone in control animals. We found that equal doses of estrone did not produce the same hepatic changes in white rats as did diethylstilbestrol. The toxicity of estrone was also observed in our animals, but the toxic dose was far greater than the toxic dose of diethylstilbestrol.

Effect of Androgens on the Blood Count of Men

DRS. E. PERRY MCCULLAGH and T. REID JONES, Cleveland: In 10 eunuchoid and 2 normal men given methyl testosterone, testosterone propionate or both the erythrocyte count, hemoglobin content and the hematocrit reading of the circulating blood were studied during periods varying from one month to eight years. In 8 of the 10 eunuchoid and in 1 of the 2 normal men these values rose with therapy, fell on withdrawal of therapy or did both. In 7 of the 9 men who responded to treatment the curve of the blood count was shown to follow approximately the curve of the basal metabolic rate. In 2 of the 7 cases in which this parallelism occurred the shift in the basal metabolic rate was more rapid than that in the blood count, while in 3 the blood count changed as rapidly as the basal metabolic rate; in 2 this relationship could not be determined. It is concluded that the changes in erythrocyte and hemoglobin levels observed with androgen therapy are related to changes in the basal metabolism and perhaps other intimately connected metabolic shifts. We believe we have reproduced a rapid form of the change in the hemopoietic system which occurs slowly in normal persons during adolescence.

DISCUSSION

DR. C. A. DOAN, Columbus, Ohio: Were reticulocyte counts, studies of the blood volume and studies of fluid excretion and intake made for these patients? Were there any alterations in the remaining blood elements?

DR. E. PERRY MCCULLAGH, Cleveland: In cases in which the white cell count was done there was no significant shift found to parallel the shift in the red cell count. Reticulocyte counts were done for 1 patient who received methyl testosterone in doses of 500 mg. a day for ten days. The reticulocyte count was obtained several times before medication and approximately on alternate days throughout medication and subsequently. No reticulocyte response was observed. Studies on the blood volume are being done now. The weight shift has not been correlated with the blood counts on the charts shown, but almost all patients gain weight when receiving injections of testosterone proprionate. The standard weight gain with methyl testosterone has not been above 20 pounds (9 Kg.), and most of this is apparently water retention, because the patient loses weight rapidly on cessation of treatment.

The Effect of the Synthetic Dicoumarin 3,3′-Methylenebis (4-Hydroxycoumarin) on the Prothrombin Time and Coagulation Time

DRS. OVID O. MEYER, JAMES B. BINGHAM and FREDERICK J. POHLE, Madison, Wis.: Link and his associates, of the Wisconsin Agricultural Experimental Station, have isolated the causative hemorrhagic agent in spoiled sweet clover disease of cattle. Further, they have recently synthesized this substance, thus making it readily available in considerable quantities for clinical study.

The substance 3,3′-methylenebis (4-hydroxycoumarin) has been administered to dogs and to human beings orally and, in the form of the sodium salt, intravenously. The administration in suitable single doses by either route is followed after a usual latent period of twenty-four hours or more by prolongation in the prothrombin time and the coagulation time, which is sustained over several days, with a gradual return to normal levels. The administration of vitamin K does not inhibit the prothrombin prolongation effect, but transfusions will temporarily restore the prothrombin time and coagulation time to normal.

Pathologic studies have demonstrated widespread dilatation of small vessels but no significant hepatic change. Tests of hepatic function have not been altered by the dicoumarin.

This material has been given in single and repeated doses to a large number of dogs and to patients with a variety of conditions in order to establish an effective but safe dose. We have found that 4 to 5 mg. per kilogram may be given intravenously or orally with safety. This dose may be repeated as necessary, the necessity being determined by the prothrombin time and the coagulation time. An alternate plan has been that of oral administration of daily doses of 1 to 1.5 mg. per kilogram after the initial larger dose. It is conceivable that the material may well have an important place in clinical medicine in the prevention of thrombosis and in other circumstances as a substitute for heparin. It has the advantages over heparin of potency when given orally and of relative inexpensiveness. On the other hand there are hazards from incautious use of this dicoumarin, for gross bleeding might occur if the dose is excessive. The effect of even a single dose is protracted and cannot be quickly neutralized except by transfusions of blood or serum.

The Effect of 3,3′-Methylenebis (4-Hydroxycoumarin) on Blood Coagulation Factors

DRS. NELSON W. BARKER, HUGH R. BUTT, EDGAR V. ALLEN and JESSE L. BOLLMAN, Rochester, Minn.: We have administered 3,3′-methylenebis (4-hydroxycoumarin) orally to 52 human subjects. This series includes 4 normal subjects, 9 patients with peripheral vascular disease associated with arterial thrombosis, 1 with subacute bacterial endocarditis, 10 with postoperative pulmonary embolism and infarction, 7 with postoperative thrombophlebitis and 21 patients with abdominal operations without vascular complications. In the last mentioned group the administration of the drug was begun on the second postoperative day.

Daily determinations of the Quick prothrombin time and the Lee-White coagulation time have been made on these patients before, during and after the administration of the drug. With a few exceptions we have noted a somewhat variable but definite increase in the prothrombin time in all cases. Increase in the coagulation time usually occurred but was considerably less consistent than the effect on the prothrombin time and not entirely parallel to it.

The most effective doses of 3,3′-methylenebis (4-hydroxycoumarin) were 300 mg. the first day and 200 mg. the second day, each given in a single dose. The elevation of the prothrombin time was usually noted on the third day, but if this did not occur

we continued to give 200 mg. daily until the prothrombin time became greater than thirty-five seconds (our normal was nineteen to twenty-two seconds). If it was felt desirable to maintain an elevated prothrombin time, a single dose of 200 mg. was given as soon as the prothrombin time became less than thirty-five seconds, and this was continued daily until the prothrombin time again became greater than thirty-five seconds. Two patients were found to be resistant to the effects of the drug in the doses mentioned.

The experimental work on animals has demonstrated that the chief hazard of the administration of 3,3'-methylenebis (4-hydroxycoumarin) is the likelihood of hemorrhage. We encountered hemorrhage in 6 cases, in all of which operation had been performed and there had not been previous evidence of thrombotic or embolic disease. In 5 the hemorrhage was minimal, and in 1 it was moderate. In all cases the hemorrhage came from operative wounds.

We have noted no other untoward effects of the drug except that in 1 case urticaria and headache developed twice after its administration.

The administration of vitamin K prior to and during the same period that 3,3'-methylenebis (4-hydroxycoumarin) was given has not prevented the elevation of the prothrombin time. After the prothrombin time has been elevated, the effect of vitamin K in restoring it to normal has been variable and somewhat inconsistent. In 6 cases blood transfusions were given when the prothrombin time was elevated. This was followed by a gradual drop in the prothrombin time to normal, usually within one to twelve hours. It was occasionally found necessary to give two or three transfusions of 500 cc. each to secure this effect, and only fresh blood was effective. There was a tendency for the prothrombin time to rise again twenty-four to forty-eight hours after it had been restored to normal by transfusion.

In none of the cases did we observe any clinical evidence of new thrombosis, extension of previously existing thrombosis, pulmonary embolism or infarction when the prothrombin time was elevated as the result of the administration of the drug. This series of cases is too small for one to draw a definite conclusion that the drug will accomplish the effect which we desire, namely the complete prevention of thrombosis and therefore of embolism. The preliminary studies indicate that 3,3'-methylenebis (4-hydroxycoumarin) may be valuable as a substitute for heparin in the treatment of many of the conditions for which heparin is now used. It possesses the obvious advantages that it is inexpensive and can be administered by mouth.

DISCUSSION ON PAPERS OF DRS. MEYER, BINGHAM AND POHLE AND DRS. BARKER, BUTT, ALLEN AND BOLLMAN

DR. ELMER L. DEGOWIN, Iowa City: I should like to ask what effect preserved blood has on the action of dicoumarin.

DR. HOWARD ALT, Chicago: Would Dr. Meyer comment on the possible mode of action of synthetic dicoumarin?

DR. ARMAND J. QUICK, Milwaukee: I should like to point out three differences between the action of heparin and that of this new substance, dicoumarin: 1. Dicoumarin requires twenty-four hours before it begins to inhibit coagulation, whereas heparin is active immediately after injection. 2. When the prothrombin concentration is once reduced by dicoumarin it can be elevated only by a blood transfusion. 3. This new material, as Dr. Meyer said, definitely has a dilating effect on the minute blood vessels, whereas no vasodilatation occurs from the injection of heparin. These three disadvantages of dicoumarin must be considered in its therapeutic evaluation. It is obvious that a simple name for the active principle of toxic sweet clover is desirable. The complete chemical name is complex, and the term dicoumarin is indefinite. I therefore suggest the term melilotoxin, since the scientific name for sweet clover is melilotus.

DR. JESSE L. BOLLMAN, Rochester, Minn.: We have found this dicoumarin compound valuable in the experimental laboratory in experiments involving cannulation of arteries and veins of dogs when delayed coagulation was necessary. We gave the dicoumarin compound four to seven days prior to the experiment. The surgical procedures were not attended by excessive bleeding, and the blood in the cannulas in arteries and veins did not thrombose during six hours of observation. Thrombosis in the cannulas would occur in untreated dogs in a few minutes; large amounts of heparin were previously necessary for these experiments. Continued use of excessive amounts of the dicoumarin is dangerous. The animals bleed spontaneously and die, since the drug is the active agent of sweet clover disease.

DR. OVID O. MEYER, Madison, Wis.: My associates and I feel that the points Dr. Quick has made are well taken. We who talk about dicoumarin are more anxious that the name be simplified than is he. We do not know the mode of action. Dr. Link feels that this material may undergo a change within the body and that during the time this occurs there is a latent period. I think the possibility that the dicoumarin acts as a physiologic inhibitor of the liver is tenable. During the latent period the prothrombin that existed in the blood is used, and when this has been completely utilized, the liver being inhibited, there is a fall in prothrombin and a prolongation of the prothrombin time. All this is of course purely theoretical. I might say that when large doses have been given by Link and his associates much of the dicoumarin has been recovered in the feces. Regardless of the dose the latent period always is observed and massive doses do not appear to have an appreciable shortening effect. It is true, however, that when the larger dose is given the effect is more protracted. As to Dr. De Gowin's question, only several days ago we gave 250 cc. of banked blood to a patient whose coagulation time was twenty-three minutes. The coagulation time within the hour fell to thirteen minutes, but the prothrombin time was not appreciably affected. Of course the actual quantity of blood was not more than 125 cc. (there being 125 cc. of preservative); so the factor of quantity as well as the factor of storage of the blood must be taken into account in the failure of any appreciable effect on the prothrombin. I do not believe that banked blood is as satisfactory as fresh blood, and Dr. Barker, I believe, has so stated in his paper.

DR. NELSON W. BARKER, Rochester, Minn.: Our experience has been that transfusion of banked blood does not produce the same effect as does transfusion of fresh blood in restoring to normal the prothrombin time of patients who have received 3,3'-methylenebis (4-hydroxycoumarin). The reasons for this are not clear, although it is probable that the prothrombin in the banked blood is destroyed or inactivated after a time. It is probable that the entire effect of the transfusion is in restoring prothrombin. The effect of the transfusion is somewhat more striking if the prothrombin time is falling than if it is rising. The exact basis for the effect of the drug on the prothrombin time is not known, but it is probable that the drug prevents the formation of prothrombin.

Undescribed Type of Erythropoiesis Observed in Human Sternal Marrow

DRS. LOUIS R. LIMARZI, SAMUEL A. LEVINSON and ROBERT M. JONES, Chicago: The observation of previously undescribed erythrocytogenesis in human sternal marrow is the subject of this report. Amitotic and multipolar erythrocytopoiesis have been observed in serially aspirated specimens of marrow from a patient dying of acute leukemic reticuloendotheliosis. With this type of erythroid development normal bipolar mitosis also occurred. In normal bone marrow only bipolar mitosis is observed, and even in cases of severe erythroid immaturity this is the only type of cell division noted. In pernicious anemia the rapid conversion of megaloblastic to normoblastic marrow which follows within twenty-four to forty-eight hours the injection of liver extract, multipolar mitoses and large multinucleated erythroid cells are not uncommonly seen. Since the normal bipolar type of mitosis and maturation does not explain this rapid change in the megaloblastic marrow, we believe that the type of erythropoiesis described may explain the change.

DISCUSSION

DR. HARRY AGRESS, St. Louis: I have observed erythropoiesis of the multipolar type in two human embryos and in a number of rat embryos. This phenomenon was not observed in older embryonic life. Dr. Limarzi's observations, together with those noted in the embryos, appear to support the belief that the erythropoiesis in pernicious anemia is of the primitive type rather than a purely functional disturbance.

(To be continued)

Current Medical Literature

AMERICAN

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Titles marked with an asterisk (*) are abstracted below.

American Journal of Medical Sciences, Philadelphia

203:1-156 (Jan.) 1942

Vascular and Cellular Dynamics of Shock. V. H. Moon, Philadelphia. —p. 1.

*Observations on Etiologic Relationship of Achylia Gastrica to Pernicious Anemia: IX. Difference in Site of Secretion of Intrinsic Factor in Hog and in Human Stomach. H. J. Fox and W. B. Castle, Boston. —p. 18.

Relationship Between Spleen and Morphologic Picture of Blood Regeneration. W. O. Cruz and Frieda S. Robscheit-Robbins, Rochester, N. Y.—p. 28.

*The Heart in Sickle Cell Anemia. H. F. Klinefelter, Baltimore.—p. 34.

Note on Cardiac Murmurs: Recommendation for Revised Terminology. P. D. White, F. D. Adams, Boston, and D. Craib, Johannesburg, South Africa.—p. 52.

Early Diagnosis of Syphilitic Aortitis. S. Boharas, L. Hollander and M. Goldsmith, Pittsburgh.—p. 54.

Histologic Kidney Changes in Common Acute Infectious Diseases. M. Kannerstein, Clarksburg, W. Va.—p. 65.

*Acute Porphyria. S. Nesbitt, New Haven, Conn., and C. H. Watkins, Rochester, Minn.—p. 74.

Phosphorus Metabolism of Blood of Patients with Leukemia and Polycythemia. L. A. Erf and L. W. Tuttle, Berkeley, Calif.—p. 83.

May the Disease Complex That Includes Megaesophagus (Cardiospasm), Megacolon and Megaureter Be Caused by Chronic Vitamin B_1 Deficiency? E. Etzel, Ann Arbor, Mich.—p. 87.

Spontaneous Beriberi of Monkey as Compared with Experimental Avitaminosis. C. P. Leblond, Rochester, N. Y., and J. Chaulin-Servinière, Casablanca, French Morocco.—p. 100.

Vitamin B_1 Not Helpful in Protracted Insulin Shock. Esther Somerfeld-Ziskind, E. Ziskind, L. Dalton and Virginia Buck, Los Angeles. —p. 110.

Studies of B Vitamins in Human Subject: III. Response of Cheilosis to Vitamin Therapy. T. E. Machella, Philadelphia.—p. 114.

Postrepeal Study of 300 Chronic Alcoholics. J. V. Lowry, Bethesda, Md., and F. G. Ebaugh, Denver.—p. 120.

Achylia Gastrica and Pernicious Anemia.—Using various preparations of hog and human stomachs, Fox and Castle attempted to determine whether the material present in the preparations and possessing a blood forming activity in addisonian pernicious anemia defined the site at which the intrinsic factor was secreted and whether observations with the hog stomach were applicable to man. The blood forming activity of desiccated preparations of the human stomach, after the arbitrary division (Meulengracht) into pylorus, fundus and cardia, had a distinctly different distribution from that obtaining in similar areas of the hog stomach. The so-called fundus and cardia preparations were definitely effective, whereas the pylorus preparation was, at best, weakly active as compared with ventriculin (New and Nonofficial Remedies). The observations confirm the validity of the experiments of Meulengracht, Ungley and others concerning the effectiveness of desiccated preparations of the pylorus and the ineffectiveness of similar preparations of the fundus portion of the hog stomach. The application of Meulengracht's assumption that the antianemic potency of the pyloric portion of the hog stomach indicates it as the site at which the intrinsic factor is secreted in that animal to the present observations with desiccated preparations of normal human stomach suggests that, in man, areas containing the fundus type of gland, and not the "pyloric gland organ," are the important sites at which the intrinsic factor is secreted. This site coincides with the site of the degenerative process seen in microscopic preparations of the stomach in pernicious anemia. Because the cardia portion of the human stomach is apparently an active site for the secretion of the intrinsic factor, gastric resections in man which preserve this portion should, theoretically, provide a source of intrinsic factor for the patient.

The Heart in Sickle Cell Anemia.—Klinefelter observed that many symptoms present during exacerbations of the disease are similar to those of acute rheumatic fever, and many cardiac signs observed during the quiescent stage resemble those of chronic valvular heart disease, particularly mitral stenosis. Twelve patients, 8 male and 4 female (aged 8 to 27, with the average age 19), with severe sickle cell anemia presented hematocrit values ranging from 20 to 30 per cent. The average duration of the anemia was eleven years. Nine of the 12 patients complained of recurring attacks of pain in the joints of the extremities. The pain sometimes involved the long bones. Several patients have had an inflammatory reaction in a joint with swelling, redness, increased heat and pain on motion. The pain usually occurred during a "crisis," which was frequently preceded by an infection of the respiratory tract. There were associated fever, icterus and leukocytosis. The pain did not respond to treatment with salicylates. None of the patients had so far exhibited frank evidence of congestive heart failure. This seems to occur only during the terminal stage. Seven of the patients have dyspnea on exertion, with or without palpitation, and 5 of these 7 are subject to recurrent ulcers of the leg; 2 other patients without exertional dyspnea have ulcers. The heart of these patients is definitely enlarged. Systolic and diastolic murmurs are common, as are a third heart sound at the apex and an accentuated second pulmonic sound with a systolic murmur at the base. The PR interval is often prolonged. The diagnosis of rheumatic heart disease has often been made in such patients, but it has not been confirmed at necropsy. The cardiac changes in sickle cell anemia are probably secondary to the severe long-standing anemia. The crisis of sickle cell anemia mimics acute rheumatic fever, but it differs in that the pain involves the long bones and is not relieved by the administration of salicylates.

Acute Porphyria.—Nesbitt and Watkins report 3 cases of acute porphyria in which the diagnosis was confirmed by the demonstration of large quantities of uroporphyrin, mostly of the isomeric series III, and 1 case in which despite the usual clinical picture of acute porphyria a diagnosis of paroxysmal hemoglobinuria was made because of spectroscopic demonstration of oxyhemoglobin in the urine and the blood serum during crises. The condition in this case might actually be acute porphyria. The absorption bands believed to be those of oxyhemoglobin were probably the bands of the zinc metal complex of uroporphyrin. The 4 cases were encountered during the last three years, suggesting that the disease is not as unusual as supposed. The disease manifests itself by one or by a combination of the following factors: a familial history, various types of gastrointestinal disturbances, abdominal pain, red or dark reddish brown urine, involvement of the central nervous system, jaundice, renal damage and, rarely, pigmentation of the skin or dermal photosensitivity.

Annals of Internal Medicine, Lancaster, Pa.

15:953-1178 (Dec.) 1941

Clinical Symptoms and Signs of Vitamin B Complex Deficiency. W. H. Sebrell, Bethesda, Md.—p. 955.

*Scarlet Fever Immunization. J. A. Toomey, Cleveland.—p. 959.

Treatment of Acute Empyema: Treatment by Continuous Tidal Irrigation and Suction (Hart). B. Klotz, Washington, D. C., and B. Lidman, Norfolk, Va.—p. 974.

*Chemotherapy of Bacterial Endocarditis. R. A. Kinsella, St. Louis.—p. 982.

*Sputum Studies in Pneumonia: Selection of Therapy. A. W. Frisch and A. E. Price, Detroit.—p. 987.

Medical Aspect of Ankylosing Spondylitis (Marie-Strümpell). W. W. Herrick and T. L. Tyson, New York.—p. 994.

Rheumatism and Arthritis: Review of American and English Literature for 1940 (Eighth Rheumatism Review). P. S. Hench, Rochester, Minn.; W. Bauer, Boston; E. Boland, Los Angeles; H. Dawson, New York; R. H. Freyberg, Ann Arbor, Mich.; W. P. Holbrook, Tucson, Ariz.; J. A. Key, St. Louis; L. M. Lockie, Buffalo, and C. McEwen, New York.—p. 1002.

Scarlet Fever Immunization.—According to Toomey, since early 1925 immunization to scarlet fever has been offered to all susceptible nurses entering the City Hospital. The Dick test was performed on 4,640 nurses, 3,104 of whom reacted negatively and 1,536 positively. Of the latter 207 were affiliate nurses who did not take contagious disease training and for whom consequently immunization was not compulsory, and of the

remainder 1,329 were actively immunized, 1,273 by inoculation with toxins in doses of 500, 2,000, 8,000, 25,000 and 80,000 units, 41 with Larson's vaccine and 15 with toxin made from stock streptococci. Of the 1,273 nurses 1,181 had negative reactions after one to five or more doses of toxins. Scarlet fever developed in 8 of the successfully immunized nurses; 131 had general reactions (malaise, nausea, headache, high fever, a scarlatiniform rash, vomiting, diarrhea, adenitis and arthritis) some time after the injection. Of 100 nurses tested five years after the first negative Dick reaction had been obtained, approximately 72 per cent still had a negative reaction. It seems that an immunization procedure which protects children 5 to 6 years of age may be sufficient to give them enough immunity so that with the additional stimulus obtained from frequent consequent exposure they may become permanently immunized against the disease. The author suggests that active immunization, though not yet a public health measure, can be used in private practice provided precautions are taken to avoid complications.

Chemotherapy of Bacterial Endocarditis. — Kinsella declares that the diagnosis of bacterial endocarditis must be based on evidence of toxemia, valvular defects, bacteremia and embolic phenomena and that bacteremia from other sources must be excluded. If one reviews the literature with these criteria in mind the number of apparent cures of the disease dwindles. During the last three years 28 patients with acute and subacute bacterial endocarditis have been treated with chemical agents at the University Hospital. Blood cultures were frequently sterilized both by merthiolate and by the sulfonamide drugs. The amount of merthiolate administered should not exceed 0.15 Gm. per hundred pounds (45.5 Kg.) of body weight. It should not be given more frequently than once in ten days, nor should it be used if active hemorrhagic nephritis is present. The sulfonamide derivatives were used in an effort to maintain the usually accepted blood levels of the drug. Two patients were treated with neoarsphenamine. There were no recoveries. The histories of 3 patients are specially mentioned. The first illustrates how standard methods instituted under apparently ideal conditions still failed to bring about a recovery. The second illustrates the possible cure of endarteritis of the pulmonary artery by merthiolate. The third illustrates the cure (observed at necropsy) of bacterial endocarditis or endarteritis by successful ligation of a patent ductus arteriosus. More observation appears necessary to determine which of the procedures (sulfanilamide, sulfapyridine and sulfanilamide therapy combined with physically induced fever and neoarsphenamine therapy), if any, is to be uniformly or occasionally successful.

Sputum Studies in Pneumonia.—Frisch and Price studied Wright stained smears of rusty sputum from patients with pneumococcic pneumonia to determine the severity of the pneumonic process. As an index of the severity the authors relied on the number of extracellular encapsulated pneumococci in the sputum. If the count exceeded 50 per field the prognosis was usually grave regardless of the therapy employed. Examination of the sputum revealed the difference in the therapeutic effects of serotherapy and chemotherapy. Usually within twelve to thirty-six hours after the administration of sulfanilamide, sulfapyridine or sulfathiazole the number of pneumococci in the sputum decreased rapidly. This effect was independent of the agglutination and phagocytosis associated with active or passive immunity. The authors treated 270 patients with proved type I, II, IV, VII and VIII pneumonia. Their sole criteria for the selection of therapy were the number of pneumococci in the sputum and the day of illness on which treatment was begun. Of 48 patients ill more than four days with less than 10 pneumococci per field who received no specific therapy none died. There were no deaths among 70 patients with a relatively mild infection (with 10 or less pneumococci per field) who had been ill three days or less and to whom specific serum was given to prevent the development of more serious pneumonia and to develop an active immunity. The incidence of bacteremia for this group was 17 per cent, and the average dose of serum was only 35,000 units. Chemotherapy was reserved for moderately and severely ill patients (with 11 to 50 pneumococci per field) whose response to treatment with serum was negligible. Of 114 such patients given chemotherapy alone only 7 died. The incidence (40 per cent) of bacteremia and that of multiple lobe involvement (46 per cent) were significantly higher than in the preceding two groups (0 to 13 per cent and 17 and 17 per cent respectively). The blood stream of 19 of the 24 patients with sputum counts exceeding 50 pneumococci per field harbored bacteria, the total leukocyte counts were low and two or more lobes of 21 were involved. They were given large doses of serum in addition to sodium sulfapyridine and sulfathiazole intravenously. In spite of the intensive treatment the mortality rate was 58 per cent. Of the remaining 14 patients who were variously treated 5 received serum initially, but subsequent specimens of sputum revealed that there were more than 10 pneumococci per field. Serotherapy was discontinued and chemotherapy was begun; 1 of these and 1 of the other 9 patients died. The authors believe that these therapeutic data support the concept that the prognosis can be postulated on the number of pneumococci present in the sputum.

Archives of Neurology and Psychiatry, Chicago

47:1-194 (Jan.) 1942

Vascular Pattern of Lesions of Multiple Sclerosis. R. S. Dow and G. Berglund, Portland, Ore.—p. 1.
Hemangioma of Vertebra Associated with Compression of Cord: Response to Radiation Therapy. L. Ferber and I. Lampe, Ann Arbor, Mich.—p. 19.
Susceptibility to Convulsions in Relation to Age: I. Influence of Acid Fuchsin on Rats of Various Age Groups. A. Fröhlich and I. A. Mirsky, Cincinnati.—p. 30.
Biochemical Disturbances in Mental Disorders: I. Anti-Insulin Effect of Blood in Cases of Schizophrenia. L. J. Meduna, F. J. Gerty and V. G. Urse, Chicago.—p. 38.
Continuous Ambulatory Insulin Shock Technic in Treatment of Schizophrenia: Report of Two Cases. P. Polatin and H. Spotnitz, New York.—p. 53.
Cerebral Fat Embolism: Clinicopathologic Study of Two Cases. N. W. Winkelman, Philadelphia.—p. 57.
Vasospasm and Focal Cerebral Ischemia: Experimental Study. F. A. Echlin, New York.—p. 77.
Avian Thiamine Deficiency: II. Pathologic Changes in Brain and Cranial Nerves (Especially Vestibular) and Their Relation to Clinical Behavior. R. L. Swank, Boston, and M. Prados, Montreal, Canada. —p. 97.
Amyloid Neuritis. J. W. Kernohan and H. W. Woltman, Rochester, Minn.—p. 132.
Section of Cephalic Third of Vagus-Spinal Accessory Complex: Clinical and Histologic Results. I. M. Tarlov, Brooklyn.—p. 141.

Archives of Pathology, Chicago

33:1-144 (Jan.) 1942

Experimental Studies in Cardiovascular Pathology: IV. Methyl Cellulose Atheromatosis and Thesaurosis. W. C. Hueper, New York.—p. 1.
Mesonephroma of Ovary: Further Studies. H. W. Jones Jr. and G. E. S. Jones, Baltimore.—p. 18.
*Oxyuriasis and Appendicitis. J. Schwarz and M. Straub, Rotterdam, Netherlands.—p. 28.
Heart in Combined Syphilitic Aortic Valvulitis and Rheumatic Heart Disease. J. R. Lisa, C. Solomon and D. Eckstein, New York.—p. 37.
Toxic Effects of Bitter Tasting Phenylthiocarbamide. C. P. Richter and Kathryn H. Clisby, Baltimore.—p. 46.
Experimental Atherosclerosis: IV. Effect of Testosterone Propionate and Estradiol Dipropionate on Experimental Atherosclerosis in Rabbits. J. B. Ludden, M. Bruger and I. S. Wright, New York.—p. 58.
Pulmonary Embolism Caused by Lead Bullet Following Gunshot Wound of Abdomen. R. Straus, Cleveland.—p. 63.
Pulmonary Embolism Caused by Liver Tissue. R. Straus, Cleveland. —p. 69.

Oxyuriasis and Appendicitis.—Schwarz and Straub examined 36 appendixes to aid in deciding whether Oxyuris vermicularis can cause lesions in the appendix which in turn form ports of entry for microbes. Eight of the appendixes harbored oxyurids, but no inflammation or changes were observed in the mucosa. There were 22 appendixes from patients 25 years of age or less with typical lesions of the mucosa. Often the oxyurids made half moon shaped impressions in the epithelium on which they lay. The epithelium was generally flattened and atrophic and in the deepest places almost endothelium-like. At the edges the cells became long and slender and stained red with acid dye. In the region of the impression a few epithelial cells might be missing, and small erosions and areas of necrosis were seen. Occasionally the oxyurids penetrated into the glands and were found deep in the recesses of the appendical mucosa. In some instances irregular defects in the glandular epithelium occurred, beneath which hemorrhage and inflammatory exudate were found. Two appendixes had worms encapsulated in their walls. In 4 other specimens nodules were found; 1 contained

part of a worm and 3 contained no recognizable oxyurids, but oxyurids were found in the appendical lumens. Nineteen of the specimens showed ulcerative appendicitis or acute or subacute periappendicitis associated with the presence of oxyurids. Oxyuris may be a primary cause of appendicitis.

Archives of Surgery, Chicago

44:1-186 (Jan.) 1942

Changes in Brain Volume During Anesthesia: Effects of Anoxia and Hypercapnia. J. C. White, M. Verlot, B. Selverstone and H. K. Beecher, Boston.—p. 1.
*Local Implantation of Sulfanilamide and Its Derivatives in Wounds: Its Relation to Wound Healing and Peritoneal Adhesions. S. P. Harbison and J. A. Key, St. Louis.—p. 22.
*Histologic Character of Undescended Testis After Puberty: Its Significance with Reference to Performance of Orchiopexy. C. E. Rea, St. Paul.—p. 27.
*Postoperative Infections of Respiratory Tract in Relation to Inhalation and Spinal Anesthesia: Study of 631 Cases. J. Lyford 3d, Baltimore.—p. 35.
*Preoperative and Postoperative Infections of Respiratory Tract in Relation to Inhalation and Spinal Anesthesia. J. Lyford 3d, Baltimore. —p. 41.
Primary Suture of Common Bile Duct in Choledocholithiasis. P. L. Mirizzi, Córdoba, Argentina.—p. 44.
Prophylactic Intraperitoneal Introduction of Crystalline Sulfanilamide: Experimental Observations. H. Laufman and Catherine E. Wilson, Chicago.—p. 55.
Large Retroperitoneal Chylous Cyst: Report of Case, with Experiments on Lymphatic Permeability. F. C. Lee, Baltimore.—p. 61.
Total Gastrectomy: Indications for Operation with Report of Four Cases. C. B. Morton 2d, University, Va.—p. 72.
Aseptic Necrosis and Bone Drilling. E. Bergmann and A. Krida, New York.—p. 81.
Inconstant Sympathetic Neural Pathways: Their Relation to Sympathetic Denervation of Upper Extremity. H. D. Kirgis and A. Kuntz, St. Louis.—p. 95.
*Wash Basin Contamination in Operating Rooms. J. K. Poppe, New Haven, Conn.—p. 103.
Two Stages of Bowel Distention: Study of Bowel Injury by Distention and Its Effect on Volume and Concentration of Blood. W. D. Gatch and J. S. Battersby, Indianapolis.—p. 108.
Rib Resection in Treatment of Scoliosis. H. L. Wenger, New York. —p. 119.
Capillary Permeability and Inflammation in Rabbits with Staphylococcic Septicemia: Experimental Study. R. H. Rigdon, Memphis, Tenn.—p. 129.
Reduced Temperatures in Surgery: II. Amputations for Peripheral Vascular Disease. L. W. Crossman, W. F. Ruggiero, V. Hurley and F. M. Allen, New York.—p. 139.
Lymphosarcoma of Rectum J. A. Tuta and P. A. Rosi, Chicago. —p. 157.
Cystic Tumor of Tongue: Report of Unusual Case. G. W. Duncan and R. A. Daniel Jr., Nashville, Tenn.—p. 164.
Combined Surgical and Physiologic Treatment of Cryptorchism: Description of Operative Procedure. R. H. Abrahamson, New York.—p. 170.

Sulfanilamide and Wound Healing.—In determining in rats the tensile strength of wounds of the abdominal wall, stomach and duodenum after the local implantation of sulfanilamide, Harbison and Key observed that there was no consistent difference between the abdominal wounds treated with sulfanilamide and control wounds. Wounds of the stomach ruptured at tensions of 70 to 140 mm., while wounds in the duodenum resisted tensions of 160 to 520 mm. of mercury. In some instances the control wounds were stronger, and in other instances the wounds in which sulfanilamide had been implanted were stronger. There was considerable difference in the strength of the wall of the viscus of the various animals. In 4 animals the normal lower part of the duodenum was tied off, and this could be ruptured by tensions of 400 to 500 mm. of mercury. Eleven day old wounds of control and experimental animals tended to reach this strength. These experiments indicated that the local introduction of sulfanilamide did not appreciably delay the healing or decrease the tensile strength of a wound. In animals in which sulfanilamide had been introduced there was less reaction around the wounds than was present in the wounds of control animals. The introduction of sulfanilamide and its derivatives did not tend to cause peritoneal adhesions.

Undescended Testis After Puberty.—Rea studied the undescended testes from 46 patients between 15 and 73 years of age. The specimens had been removed at necropsy or at operation because of atrophy, pain, suspected tumor, inability to bring the retained testis into the scrotum, large associated hydrocele or hernia. Atrophy, which usually was progressive with age, was observed microscopically, in all the specimens. Spermatogoniums were observed in 17, primary spermatocytes in 13, secondary spermatocytes in 8 and spermatids in 3. Spermatozoa were not seen. Spermatids were observed in undescended testes from persons in the third, fourth and seventh decade of life. The germinal epithelium in 2 undescended testes near the external inguinal ring from patients in the sixth and seventh decades of life was fairly well preserved. Because patients with bilateral cryptorchism up to 24 years of age have shown spermatozoa in the semen and because a scrotal position is necessary for continued function, the author feels that orchiopexy may be performed on selected patients with undescended gonads as late as the third decade of life. Less than 5 per cent of the patients with cryptorchism had any preserved germinal epithelium. Only if the testis is of good size and is located near the external ring should orchiopexy be considered for older patients with cryptorchism.

Postoperative Infections of Respiratory Tract.—Lyford states that the incidence of infections of the respiratory tract after inhalation and spinal anesthesia for abdominal operations in patients without such infections preoperatively was 5.8 per cent for ether, 4.9 per cent for cyclopropane and 7.5 per cent for spinal anesthesia. The incidence was unaffected by the patient's age or sex, the length of the operative anesthesia, the preoperative complications, the spinal anesthetic agent, the preanesthetic medication or the changes in blood pressure during anesthesia.

Preoperative and Postoperative Acute Infection of Respiratory Tract and Anesthesia.—Lyford points out that the incidence of acute infection of the respiratory tract rose if low grade chronic infections of the respiratory tract, not generally considered to contraindicate even elective operations, existed preoperatively. The incidence among 120 patients with such infections was 13.5 per cent for ether, 17.5 per cent for cyclopropane and 39.5 per cent for spinal anesthesia.

Wash Basin Contamination in Operating Rooms.—Poppe studied the bacterial contamination of basins filled with sterile water. Some of these basins remained sterile when exposed to the air of the room for as long as three and a half hours. Of the total number of basins studied the fluid in 56 per cent, or in 76 per cent when an antiseptic solution was not used, showed from 1 to 50 viable organisms per cubic centimeter. This is in decided contrast to the absence of viable bacteria in all the cultured samples from basins containing zephiran (a disinfectant solution). The absence of any bad infections of wounds in the cases studied by Poppe is surprising in view of the high bacterial contamination of the wash basins. However, 46 per cent of the wounds were drained, and this probably eliminated some of the potential infection. In 36 per cent of the cases in which the wound was not drained the basin was contaminated. Apparently the average incision is able to combat a large amount of contamination.

Bulletin of Johns Hopkins Hospital, Baltimore

69:493-592 (Dec.) 1941

Creatinuria Induced by Methyl Testosterone in Treatment of Dwarfed Boys and Girls. L. Wilkins, W. Fleischmann and J. E. Howard, Baltimore.—p. 493.
Accuracy of Clinical Measurements of Arterial Blood Pressure, with Note on Auscultatory Gap. C. Ragan and J. Bordley 3d, Baltimore.—p. 504.
Effects of Intra-Arterial Injection of Acetylcholine and Prostigmine in Normal Man. A. M. Harvey, J. L. Lilienthal Jr. and S. A. Talbot, Baltimore.—p. 529.
Observations on Nature of Myasthenia Gravis: Phenomena of Facilitation and Depression of Neuromuscular Transmission. A. M. Harvey, J. L. Lilienthal Jr. and S. A. Talbot, Baltimore.—p. 547.
*Id.: Intra-Arterial Injection of Acetylcholine, Prostigmine and Adrenalin. A. M. Harvey and J. L. Lilienthal Jr., Baltimore.—p. 566.

Nature of Myasthenia Gravis.—Harvey and Lilienthal studied the influence of the intra-arterial injection of varying amounts of acetylcholine and other substances on the course of myasthenia gravis in 8 patients. Injection of prostigmine methylsulfate resulted in an almost immediate increase in the strength of grip and other movements in the extremity treated. When the sphygmomanometer cuffs obstructing the venous return from the arm had been deflated, power returned to the other myasthenic muscles. The increase in power lasted three to five hours. With one exception there were no visible fasciculations in the muscles of the injected extremity or elsewhere in the

body. The injection of acetylcholine produced a severe, brief, burning pain and a prolonged flushing and sweating in the treated extremity. A few seconds after the injection the fingers, the hand and wrist became flexed. The flexion resembled the carpal spasm of tetany. During the ten to fifteen seconds that the contraction persisted the authors were unable to extend the patient's fingers and wrist. There was no observable change in the strength of grip after the involuntary acetylcholine contraction disappeared. The data indicate that the fibers of a myasthenic muscle retain the capacity for vigorous contraction when adequately stimulated, affording indirect evidence that a defect in nervous or neuromuscular conduction rather than a primary muscular disorder is responsible for myasthenia. In 1 patient injection of epinephrine during a period of profound weakness increased the motor power of the injected arm for thirty or more minutes, but there were no visible involuntary movements. This patient, who was unable to make a fist or to approximate the thumb and second finger, easily effected these finger movements after the injection, although his grip remained feeble. The increase in motor power did not approach that seen after treatment with prostigmine methylsulfate. No generalized improvement of the myasthenic symptoms followed the injection. The same patient received 15 mg. of ephedrine sulfate orally six times a day for four days; the moderate increase in general motor power that followed was real. On the fourth day 0.6 mg. of epinephrine was again injected into the brachial artery; there was a moderate but definite increase in motor power in the injected extremity only. There was no apparent augmentation or prolongation of the epinephrine effect by the ephedrine. In all instances the intra-arterial injection of epinephrine produced cooling, blanching and cyanosis of the extremity and caused the radial pulse to disappear. The similarity between the distribution of muscle weakness in myasthenia gravis and that produced by partial curarization suggests that a circulating inhibitor substance may be responsible for the primary neuromuscular defect. The substance may arise from the thymus. Blalock, Mason, Morgan and Riven reported cure of severe myasthenia gravis by removing a cystic tumor from the thymic region. Some definite abnormality of the thymus gland is observed at necropsy in a significant number of patients with myasthenia gravis. Extirpation of the thymus in patients with severe myasthenia gravis may be worthy of trial.

California and Western Medicine, San Francisco

55:279-336 (Dec.) 1941

Spinal Lesions: Their Early Signs and Importance in Diagnosis. R. B. Raney, Los Angeles.—p. 284.
Low Back Pain: Rationale of Fasciotomy in Its Treatment. K. O. Haldeman and R. Soto-Hall, San Francisco.—p. 287.
Syphilis: Interpretation of Serologic Reactions. G. V. Kulchar, San Francisco.—p. 290.
*Vitamin E and Nervous Diseases. R. W. Harvey and Portia Bell Hume, San Francisco.—p. 293.
Professional Preparedness. R. A. Pfaff, Los Angeles.—p. 295.
Visual Disturbances Following Head Injury. W. T. Grant, Los Angeles. —p. 298.
Asphyxia Neonatorum. G. Bates, San Francisco.—p. 301.
Medical Aid in the Soviet Union Army. C. L. Rubenstein, San Francisco.—p. 304.
Teaching of Dermatology: Its Development in San Francisco. D. W. Montgomery, San Francisco.—p. 305.

Vitamin E and Nervous Diseases.—Harvey and Hume gave alpha-tocopherol for forty to four hundred and eighteen days to patients with neuromuscular disease. Of 16 patients with amyotrophic lateral sclerosis the progress of the disease in 4 was checked after treatment, suggesting but not proving the possibility of arrest. Of 9 patients with progressive muscular atrophy 1 showed slight clinical improvement. Of 20 patients with progressive muscular dystrophy 4 showed slight to moderate clinical improvement, while in none was there any objective evidence of further progress of the disease. Two of 3 patients with congenital amyotonia showed improvement which probably should be attributed to spontaneous recovery. Of 3 patients with dystrophic myotonia and 1 with dermatomyositis none were improved. Two of 18 patients with multiple sclerosis had remissions of six and twelve months. The improvement could not be attributed to the treatment. The most that can be expected from vitamin E therapy is arrest of the disease process.

Connecticut State Medical Journal, Hartford

5:871-948 (Dec.) 1941

Medicine and the Antitrust Act: Discussion of Government's Suit Against American Medical Association. W. H. Hamilton, New Haven.—p. 873.
*Problem of Gastric Ulcer. S. M. Jordan, Boston.—p. 879.
X-Ray Examination of 8,210 Selectees at Induction Center, Hartford. P. S. Phelps and Helen M. Green, Hartford.—p. 882.
How To Overcome Smoking Habit. E. Kahn and E. F. Gildea, New Haven.—p. 886.
What We Can Learn from Gastroscopy. J. Flexner, New York.—p. 889.
Prospect for Patients with Large Bowel Cancer in Connecticut. A. W. Oughterson, New Haven.—p. 890.
What Happens to the Patient with Carcinoma of Colon and Rectum? W. Mendelsohn, New Haven.—p. 890.
What May Be Accomplished in Treatment of Cancer of Colon and Rectum. A. W. Oughterson, New Haven.—p. 892.
How Treatment of Carcinoma of Colon and Rectum May Be Improved. J. F. Burke, Waterbury.—p. 893.
Mortality in Diabetic Coma. A. Labensky, New London.—p. 898.
Origin of Connecticut State Medical Society. C. Barker, New Haven. —p. 900.

Problem of Gastric Ulcer.—Jordan points out that in the diagnosis of peptic ulcer it is imperative to determine whether there is an actual ulcer present or whether the symptoms are due to another organic or functional disease. The diagnosis of a functional condition (habitual pylorospasm and hyperchlorhydria) as a forerunner of ulcer is valuable because it may aid in preventing ulcer. If an ulcer is present it is necessary to know whether it is in an active or a healed state. All three types of peptic ulcer are amenable to the same medical or surgical regimen. Rest and neutralization affect favorably the causative agents, spasm and hyperchlorhydria. If rest and neutralization are intensive enough before the ulcer penetrates into neighboring structures the peptic ulcer in any location will heal. To be effective, surgical treatment which removes the actual lesion and prevents a recurrence must be carried out so that neither spasm nor hyperchlorhydria causes a recurrence. In gastric ulcer, in contrast with the duodenal and jejunal type, there is an added danger of confusing a benign, a malignant or a potentially malignant lesion. An ulcer of the posterior wall of the stomach, whether of the media or of the prepyloric area, is most difficult to find and to follow, and its healing may be interfered with because of penetration into the pancreas. In the gastric ulcer, subacute perforation and repeated hemorrhage indicate difficult and only temporary healing and should be regarded as conducive to chronic irritation in the stomach, where malignant changes occur so often. The recurrence of a gastric ulcer is a criterion for possible malignant changes in doubtful cases. Other criteria are failure of occult blood, symptoms and roentgen defects to disappear. Sometimes gastric carcinoma supervenes on a gastric ulcer which has healed incompletely or has recurred, and for this reason complete healing of a gastric ulcer should be assured and the most exacting technic be employed to detect incomplete healing.

Hawaii Medical Journal, Honolulu

1:1-72 (Sept.) 1941. **Partial Index**

Rheumatic Heart Disease in Hawaii. S. E. Doolittle and I. L. Tilden, Honolulu.—p. 7.
Kahili Flower (Grevillea Banksii) Dermatitis: Preliminary Report. H. L. Arnold Jr., Honolulu.—p. 15.
Lobectomy for Bronchiectasis. R. L. Hill, Honolulu.—p. 20.

1:1-60 (Nov.) 1941

Extrapleural Thoracoplasty in Treatment of Pulmonary Tuberculosis: Report of Series of 105 Patients. Staff of the Leahi, Home, Honolulu. —p. 7.
*Epidemic Infectious Conjunctivitis. W. J. Holmes, Honolulu.—p. 11.
*Syphilis and Neurosyphilis in Hawaii: Incidence and Results of Treatment in Territorial Hospital for Mental Disorders. R. D. Kepner, Kaneohe, Oahu.—p. 13.
Kidney Injuries. P. S. Irwin, Honolulu.—p. 20.
Mild Abdominal Pain Due to Ovulation. H. E. Bowles, Honolulu. —p. 23.

Epidemic Infectious Conjunctivitis.—Holmes discusses the rapidly spreading type of acute conjunctivitis that raged in Oahu in the summer of 1941. The condition was referred to by the patient and his physician as "pink eye." The extreme contagiousness of the disease suggested that it might be assum-

ing epidemic proportions. Repeated cultures and smears of the conjunctival scrapings and secretions from 50 unselected patients failed to reveal any organism. It was surmised that a virus is the underlying etiologic agent. The swimmer, the worker in the pineapple cannery, the worker at the emery wheel and the patient with a preexisting ocular disease felt that the particular environment was responsible for the disease. In all cases there was the common factor of rubbing the eyes with dirty fingers. The hand to eye and the eye to hand transmission was further suggested by the involvement of the second eye in three fourths of the patients and the frequent occurrence of the conjunctivitis in more than one member of a family. A contributing factor toward the spread of the disease was the recent great increase in the military and naval personnel, who lived and worked in close contact with one another. At the end of June the disease was widespread, and people from all walks of life, irrespective of age, sex and race, were affected. New infections are still encountered, but the peak has been reached. After an incubation period of two to five days the symptoms are lacrimation, burning, redness, some pain, sensitivity to light and foreign body sensation. A moderate degree of blepharospasm was encountered. Multiple subconjunctival hemorrhages appeared on the tarsal portions of the conjunctivas. Preauricular adenopathy was noticed in about 50 per cent of the patients. Ciliary injection and corneal infiltration often accompanied the superficial inflammation. When the corneal lesions developed, vision was correspondingly reduced and patients also complained of seeing halos around lights. When corneal complications were absent the average duration of the disease was two to three weeks; if they were present the irritation remained for four to six weeks or longer. The various therapeutic remedies usually employed for conjunctivitis were more or less ineffectual. Keeping the patient in a dark room proved most beneficial. Cold compresses afforded more relief than hot applications. Bland lotions and ointments were used for symptomatic relief.

Syphilis and Neurosyphilis in Hawaii.—Kepner states that the percentage of patients with syphilis admitted for the first time to the Territorial Hospital for mental diseases has shown a gradual decline since 1923. The incidence of first admissions for syphilis in one form or another was 17.9 per cent. Of the 582 syphilitic patients admitted 438 were men and 144 were women. This sex ratio compares with first admissions from 1923 to 1940 and with the population of the territory. The incidence (8.4 per cent of the total of syphilitic patients admitted) of neurosyphilis in the hospital compares favorably with that in hospitals on the mainland. Patients with meningovascular syphilis were treated with preparations of heavy metals, arsenicals and iodides. If no improvement followed in six months, tryparsamide or fever therapy or both were tried. Patients with meningoencephalitis or dementia paralytica were treated with a combination of tryparsamide and fever therapy in addition to routine chemotherapy. Improvement or pronounced improvement was noticed in 33.7 per cent of patients receiving drugs only, in 47 per cent after treatment by all methods, in 60 per cent after inductodiathermy and chemotherapy and in 69.2 per cent after typhoid shock and chemotherapy. Earlier treatment of these patients, before the damage to the cerebral parenchyma has become irreparable, would probably improve the results. To that end a spinal puncture should be performed on every patient with syphilis at least once in the course of treatment, preferably in the first year of the disease, and another when treatment is concluded. Invasion of the nervous system probably occurs in all patients with early syphilis. The spinal fluid of any patient under treatment for syphilis who displays unusual irritability, mental dulness, loss of weight, forgetfulness, sleepiness, speech defects, insomnia, judgment defects, fatigability, digestive defects, definite visual impairment, occasional headaches or rheumatoid pains should be examined. To reduce the development of neurosyphilis to a minimum it is necessary to treat early syphilis adequately. If, in addition, signs and symptoms of neurosyphilis are looked for it will be possible to institute proper therapy early, and thus many useful and productive years may be added to the life of the afflicted person.

Indiana State Medical Assn. Journal, Indianapolis

35:1-58 (Jan.) 1942

Industrial Health. C. D. Selby, Detroit.—p. 1.
Polycystic Disease of Liver. W. D. Inlow and N. F. Richard, Shelbyville.—p. 4.
Complications of Mastoiditis. J. R. Swan, Indianapolis.—p. 9.
After-Treatment of Poliomyelitis. R. B. Acker, South Bend.—p. 14.
Clinical Application of Newer Laboratory Procedures as Pertains to the Man in General Practice. J. O. Ritchey, Indianapolis; A. S. Giordano, South Bend; W. Dodds, Crawfordsville, and G. B. Wilder, Anderson.—p. 17.
Gaseous Indigestion. C. O. Richey, Evansville.—p. 21.
Surgical Lesions of Kidney—Their Differential Diagnosis, with Note on Management. E. Rupel, Indianapolis.—p. 23.

Journal of Experimental Medicine, New York

74:511-648 (Dec.) 1941

Studies on Reactions Relating to Carbohydrates and Polysaccharides: LXIV. Antigenicity of Dextran Produced by Leuconostoc Mesenteroides. T. H. Evans, W. L. Hawkins and H. Hibbert, Montreal, Canada.—p. 511.
*Natural History of Human Poliomyelitis: II. Elimination of Virus. A. B. Sabin and R. Ward, Cincinnati.—p. 519.
Inactivating Effect of Sulfapyridine on Leukotoxic Action of Benzene. M. McCarty and W. S. Tillett, New York.—p. 531.
Quantitative Study of Scarlet Fever Toxin-Antitoxin Flocculation Reaction. G. A. Hottle and A. M. Pappenheimer Jr., Philadelphia.—p. 545.
Capacity of Pleuropneumonia-like Micro-Organisms to Grow on Chorioallantoic Membranes. H. F. Swift, New York.—p. 557.
Determination of Volume of Extracellular Fluid of Body with Radioactive Sodium. N. L. Kaltreider, G. R. Meneely, J. R. Allen and W. F. Bale, Rochester, N. Y.—p. 569.
Effect of High Protein Diets on Experimental Renal Hypertension. H. Philipsborn, L. N. Katz and S. Rodbard, Chicago.—p. 591.
*Occurrence of Poliomyelitis Virus in Autopsies, Patients and Contacts. J. F. Kessel, F. J. Moore, F. D. Stimpert and R. T. Fisk, Los Angeles.—p. 601.
Bactericidal Action of Synthetic Detergents. Zelma Baker, R. W. Harrison and B. F. Miller, with technical assistance of R. Wexler, Chicago.—p. 611.
Inhibition by Phospholipids of Action of Synthetic Detergents on Bacteria. Zelma Baker, R. W. Harrison and B. F. Miller, with technical assistance of R. Wexler, Chicago.—p. 621.

Natural History of Human Poliomyelitis.—Sabin and Ward studied the excretion of the virus of infective poliomyelitis from the human body during the first two weeks of the paralytic illness. They also attempted to discover the origin of the eliminated virus. While the virus could be demonstrated with considerable regularity in the stools (especially in children less than 8 years old), it was not obtained from a single nasal (not nasopharyngeal) secretion or oral secretion and saliva or from large amounts of urine. The hypothesis that virus is present in the stools because it has been swallowed with nasal or other secretions of the upper respiratory tract becomes untenable, and as it is present in the walls of the alimentary tract its origin from this site is much more probable. The negative results obtained with nasal secretions may be due to the presence of an inactivating substance and need not necessarily indicate that the virus is absent. However, studies suggest that the virus neither multiplied in the nervous system nor invaded it by way of the nose because, while it was readily demonstrated in the pharyngeal and intestinal tissue, it was not present in the nasal mucosa or in the olfactory bulbs of the patients studied. No support was found for the hypothesis that poliomyelitis virus in the stools originates from swallowed nasal and oral secretions.

Poliomyelitis Virus in Patients and Contacts.—Kessel and his co-workers summarize their attempt to recover the virus of poliomyelitis from the cord, medulla, colonic contents and urine at the necropsy of patients, from the cerebrospinal fluid, nasal washings and stools of living patients and from the stools of contacts. They have recovered poliomyelitis virus from the spinal cords of 50 per cent of monkeys, from the olfactory bulbs of 10 per cent and from tonsil-adenoid tissue of 50 per cent; they recovered the virus at necropsy from the colonic contents of 26 per cent of patients and from the stools of 20 per cent of living patients and from the stools of 5 per cent of the contacts examined. The virus was not recovered from the hypophysis, mesenteric lymph node, thymus, Peyer's patch, bile and urine at necropsy or from the cerebrospinal fluid (questionable in 1) or the urine of 134 living patients. The spinal cords, tonsil-adenoid tissue or the colonic contents were positive for the virus in 73 per cent of the necropsies. The virus was isolated from the stools of 22 per cent of patients with paralysis and from the

stools of 19 per cent of patients without paralysis. Of stools from 35 patients less than 16 years of age 40 per cent yielded virus, while 8 per cent of stools from 38 patients older than 15 yielded virus. At necropsy the cords of 71 per cent of 35 patients less than 16 yielded virus, while the percentage for patients of 16 or older was 31. Repeated study of the stools of 5 patients one month after the first positive stool did not disclose the virus. The stool of 1 contact was positive during the second month after first recovery of the virus, but it was negative during the third month.

Journal of Immunology, Baltimore

42:369-536 (Dec.) 1941

Experimental Investigation of Immunologic Mechanism as Cause of Glomerulonephritis. C. F. Kay, P. F. Lucchesi and R. B. Rutherford, Philadelphia.—p. 369.

Quantitative Studies on Group Specific Substances in Human Blood and Saliva: II. Group Specific Substance A, with Special Reference to Subgroups. A. S. Wiener and I. Kosofsky, New York.—p. 381.

Passage of Antipneumococcus Antibodies into Pleural Exudates in Rabbits—Comparison of Penetration of Pleura by Horse and Rabbit Serum. J. W. Haviland and J. F. A. McManus, Baltimore.—p. 395.

Occurrence of Salmonella Antigens in Dysentery Bacilli. S. Bornstein, Brooklyn; I. Saphra and J. B. Daniels.—p. 401.

Influence of Collodion Particles on Visible End Point in Antibody Titrations. D. M. Eisler, Lansing, Mich.—p. 405.

Test of Alternation ("Lattice") Hypothesis with Divalent and Trivalent Haptens. S. B. Hooker and W. C. Boyd, Boston.—p. 419.

Studies on Mechanism of Action of Sulfanilamide: V. Dissociation of Phenomena of Growth Stimulation and Sulfanilamide Inhibition of Hemolytic Streptococci. Helen M. Lynch and J. S. Lockwood, Philadelphia.—p. 434.

Immune Response of Mice to Active Virus and to Formalin Inactivated Virus of Eastern Equine Encephalomyelitis. Isabel M. Morgan and P. K. Olitsky, New York.—p. 445.

Descriptive Therapy of Specific Precipitation: Parts I, II and III. A. D. Hershey, St. Louis.—p. 455.

Journal of Nat. Cancer Inst., Washington, D. C.

2:201-308 (Dec.) 1941. **Partial Index**

Metabolism of Chicken Tumors. D. Burk, H. Sprince, J. M. Spangler, E. A. Kabat, J. Furth and A. Claude.—p. 201.

Quantitative Induction of Tumors in Mice with Ultraviolet Radiation. H. F. Blum, J. S. Kirby-Smith and H. G. Grady.—p. 259.

Liver Catalase Activity of Tumor Bearing Rats and Effect of Extirpation of Tumors. J. P. Greenstein, W. V. Jenrette and J. White.—p. 283.

Relative Enzymatic Activity of Certain Mouse Tumors and Normal Control Tissues. J. P. Greenstein, W. V. Jenrette, G. B. Mider and H. B. Andervont.—p. 293.

Note on Transfer of Strain C3H Milk Influence Through Successive Generations of Strain C Mice. H. B. Andervont.—p. 307.

Journal of Pharmacology & Exper. Therap., Baltimore

73:363-472 (Dec.) 1941. **Partial Index**

Method for Rapid Isolation and Spectrographic Measurement of Cocaine from Brain Tissue. L. A. Strait, R. B. Aird and S. Weiss, San Francisco.—p. 363.

Mode of Action of Sulfonamides: II. Specific Antagonism Between Methionine and Sulfonamides in Escherichia Coli. J. S. Harris and H. I. Kohn, Durham, N. C.—p. 383.

*Use of Clorarsen in Treatment of Syphilis. R. R. Tompsett, W. G. Downs, W. McDermott and B. Webster, New York.—p. 412.

Comparison of Calcium Acetylsalicylate (as Calcamate) with Acetylsalicylic Acid. J. W. Stutzman, O. S. Orth and C. H. Mellish.—p. 420.

Effect of Metrazol on Blood Pressure of Man and Dog. R. A. Woodbury, W. F. Hamilton, H. M. Cleckley and P. P. Volpitto, Augusta, Ga.—p. 431.

Action of Drugs Beneficial in Myasthenia Gravis: I. Effect of Prostigmine and Guanidine on Serum and Muscle Potassium. V. Thompson and A. Tice, Iowa City.—p. 455.

Effects of Mecholyl, Potassium Chloride and Prostigmine on Neuromuscular Atrophy and Regeneration. H. M. Hines, J. D. Thomson and B. Lazere, Iowa City.—p. 463.

Sulfapyridine (2-Sulfanilamidopyrazine): Its Antipneumococcic Activity as Compared with That of Sulfapyridine, Sulfathiazole and Sulfadiazine. L. H. Schmidt, J. M. Ruegsegger, Clara L. Sesler and M. Hamburger Jr., Cincinnati.—p. 468.

New Drug for Syphilis.—Tompsett and his associates investigated the antisyphilitic properties of 3-amino-4-hydroxyphenyl dichlorarsine hydrochloride, known as clorarsen. The probable toxicity of the drug was determined in mice and rabbits, and no lesions were found in killed animals that could be attributed to the toxic effect of the drug. The clinical material for the study consisted of 171 patients treated over two years; 117 had early and 38 had late latent syphilis; 4 had asymptomatic neurosyphilitic and 12 had various syphilitic lesions. The general scheme of treatment was that of the usual combined bismuth and arsenical treatment except that treatment with clorarsen was generally prolonged to ten or twelve injections. Forty-eight hours after one injection of 0.045 Gm. of clorarsen the surface organisms on dark field examination were usually not present in the lesion. Healing of the primary and secondary lesion was prompt and compared favorably with that following treatment with the standard arsenical drugs. The serologic response of 50 patients with early syphilis to clorarsen therapy was followed by means of the Wassermann reaction at the inception of therapy and at the end of each course. In 40 the positive serologic reaction was reversed within less than six months and in 7 within six to twelve months, and the reaction of 3 is still positive after more than six months of therapy. Of the patients with late syphilis who have received more or less continuous therapy, 10 have had serologic reversal within twelve months. Ten others are considered seroresistant in that they have been treated for more than one year without a reversal of the serologic reaction. In 7 of these there has been a definite decrease in the titer of reagin. The spinal fluid of 33 of 34 patients with early syphilis after more than six months of therapy was negative, and that of 1 was a definite group II fluid nine months after treatment had been begun. Only 1 patient had an infectious relapse. Serologic relapse was not encountered. Gastrointestinal, cutaneous and syncopal reactions occurred in 51 patients. There were no severe immediate reactions.

Journal of Urology, Baltimore

46:1051-1164 (Dec.) 1941

Conservative Surgery of Hydronephrosis: Analysis of Results Obtained by Various Procedures. V. J. O'Conor, Chicago.—p. 1051.

Surgical and Nonsurgical Management of Renal and Ureteral Calculi. J. H. Sanford and W. T. Barnhart, St. Louis.—p. 1061.

Clinical Study of Two Unusual Types of Renal and Ureteral Disease. C. H. deT. Shivers and J. H. Mathis, Atlantic City, N. J.—p. 1079.

*Tumor of Suprarenal Medulla Associated with Paroxysmal Hypertension: Report of Case Preoperatively Diagnosed and Cured by Surgical Removal. J. J. Crane, L. A. Alesen and E. L. Touriel, Los Angeles.—p. 1100.

Limitations of Irradiation of Solid Renal Tumors in Children. H. O. Mertz, R. D. Howell and J. W. Hendricks, Indianapolis.—p. 1103.

*Leiomyosarcoma of Prostate: Report of Case and Critical Review. C. L. Prince and S. A. Vest, Charlottesville, Va.—p. 1129.

Irradiation Control of Testicular Tumor Metastases: Return of Renal Function After Long Apparent Absence. A. Randall, Philadelphia.—p. 1144.

Experimental and Clinical Evidence on Role of 17-Ketosteroids in Prostatic Carcinoma. R. W. Satterthwaite, Justina H. Hill and Elizabeth F. Packard, Baltimore.—p. 1149.

Tumor of Adrenal Medulla.—Crane and his co-workers report the cure of a man of 52 who had had paroxysmal hypertension for nine years by the surgical removal of a pheochromocytoma of the right adrenal gland. The tumor was removed through a lumboposterior incision, after it and the normal left adrenal gland had been palpated through a midline abdominal incision.

Leiomyosarcoma of Prostate.—Prince and Vest present the fifteenth case of leiomyosarcoma of the prostate to be cited in the literature and the first, they believe, in which the condition was diagnosed preoperatively. The specimen, which included the entire prostate (which was definitely larger than normal, especially on the right) was removed through a perineal incision according to the technic of Young. The patient, when last seen, one year after the operation, was in excellent health and had no complaints. He had gained weight and was working every day. On rectal examination there was no induration in the region of the bladder or the triangular ligament. Roentgenograms showed no evidence of metastasis. The cause of prostatic leiomyosarcoma is not known, and its relationship to benign leiomyoma of the prostate has not been proved.

Kansas Medical Society Journal, Topeka

42:501-540 (Dec.) 1941

Pathogenesis of Cholecystitis. N. A. Womack, St. Louis.—p. 501.

Reporting of Tuberculosis in Kansas. F. C. Beelman, Topeka.—p. 506.

Problems in Therapy of Intractable Asthma. A. J. Brier, Topeka.—p. 508.

The Psychiatrist in Relation to the Local Selective Service Board. W. C. Menninger, Topeka.—p. 512.

Epigastric Hernia in a Child. M. A. Walker, Kansas City.—p. 515.

Ascorbic Acid in Treatment of Arsenical Dermatitis. M. Delp, Kansas City.—p. 519.

Laryngoscope, St. Louis

51:1073-1142 (Dec.) 1941

Abstracts from Literature Relating to Conditions of Trachea and Bronchi. C. J. Imperatori, New York.—p. 1073.
Present Conception of Gradenigo Syndrome. L. M. Hubby, New York.—p. 1085.
Development of Audiometer. C. C. Bunch, St. Louis.—p. 1100.
Pontofacial Angle Tumors, with Particular Reference to Involvement of Acoustic Nerve. J. H. Globus, New York.—p. 1119.

Minnesota Medicine, St. Paul

24:1021-1114 (Dec.) 1941

What Should Be Done with Acute Cholecystitis? R. W. McNealy, Chicago.—p. 1035.
Report of State Chairman Committee on Medical Preparedness of American Medical Association. F. L. Smith, Rochester.—p. 1043.
The Doctor in the New Army. J. R. Hall, Washington, D. C.—p. 1045.
Nutrition and National Defense. R. M. Wilder and R. D. Williams, Rochester.—p. 1049.
Physical Defects of Selectees. R. B. Hullsiek, St. Paul.—p. 1052.
Medical Officers of the Future. H. S. Diehl, Minneapolis.—p. 1055.
*Chemotherapy in Treatment of Streptococcic Infections. W. E. Herrell and A. E. Brown, Rochester.—p. 1059.
*Chemotherapy in Acute Otitis Media and Mastoiditis. J. F. Curtin, Minneapolis.—p. 1063.
Our Aging Population. J. F. Norman, Crookston.—p. 1066.

Chemotherapy for Streptococcic Infections.—Herrell and Brown state that the variability of the response of the different strains of streptococci to the sulfonamide derivatives make the selection of the proper drug the most important factor in successful chemotherapy. The dose and the method of administration are next in importance. Sulfanilamide, given orally or subcutaneously, remains the drug of choice for the treatment of infections due to the group A hemolytic streptococcus, and sulfanilamide or azosulfamide for the group B infections. For the average adult with a group C infection 2 or 3 Gm. of a sulfonamide derivative usually will produce adequate urinary concentrations. For infections due to the viridans group of organism either sulfanilamide or sulfapyridine is indicated, provided the organism is not an enterococcus or Streptococcus fecalis, against which the thiazole derivatives are effective. The proper compound may be used locally for the management of streptococcic infections as a prophylactic agent against infection or to treat an already existing infection in superficial tissue or in a cavity of the body. Since the isolation of gramicidin, a substance isolated from a soil bacillus by Dubos, much interest has been aroused concerning its use for infections due to the gram-positive organism for which it is a highly effective bacteriostatic agent. Recent observations concerning its hemolytic effect render the substance unsafe for general use. If the hemolytic property of gramicidin can be removed and its bacteriostatic effect preserved, an entirely new approach may ensue in the treatment of streptococcic infections and those associated with other gram-positive pathogenic bacteria.

Acute Otitis Media and Mastoiditis.—Curtin reports on 40 patients with otitis media subjected to chemotherapy and 20 treated without drugs. Of the 40, 19 harbored Streptococcus hemolyticus and 5 the pneumococcus, and from 16 no definite organism was recovered. The patients were given large initial doses of sulfanilamide, and the therapy was continued for a week after the temperature, tenderness, leukocytosis, pain and edema subsided. For the group with streptococcic infections three mastoidectomies were performed, for the group with pneumococcic infections one operation and for those showing no organism two operations. In the untreated group the streptococcus was recovered from 9 and the pneumococcus from 3, but no organism was recovered from 8. Five patients had an operation. The figures show a 10 per cent statistical advantage in favor of chemotherapy. There is sufficient evidence to indicate that chemotherapy can shorten the course of the disease and prevent many complications. For streptococcic infections a large initial dose, 1.6 to 2 Gm., of sulfanilamide should be given, followed by 1 Gm. every four hours for three or four days. If the temperature drops and the discharge diminishes, the daily dose can be reduced to 2.6 to 3.2 Gm. for a few days and then to 1.3 Gm. a day for a few days. Chemotherapy should be continued for six or seven days after the symptoms subside to avoid a recurrence. For pneumococcic infections smaller doses of sulfathiazole are given; for acutely ill children the dose is 0.13 Gm. per pound followed by a maintenance dose of 0.065 Gm. per pound. If the desired results are not obtained the level of the drug in the blood should be checked, as in some patients it does not become optimal with this dose. Antibacterial serum is often a valuable addition to the chemotherapy.

New England Journal of Medicine, Boston

225:929-962 (Dec. 11) 1941

The Private Physician's Opportunity in Industrial Medicine. J. J. Bloomfield, Bethesda, Md.—p. 929.
Clinical Classification and Diagnosis of Hemorrhagic Diatheses. W. C. Moloney, Boston.—p. 933.
*Undulant Fever in Massachusetts. R. F. Feemster, Boston, and G. A. Hyder, Lawrence, Mass.—p. 937.
Community Supervision of Mental Defectives in Massachusetts. N. A. Dayton and M. A. Nugent, Boston.—p. 941.
Diabetes Insipidus in One of Twins. H. Blotner, Boston.—p. 946.
Industrial Hygiene. S. S. Pinto and M. Bowditch, Boston.—p. 949.

Undulant Fever in Massachusetts.—Feemster and Hyder state that, since undulant fever was made reportable in 1930, 331 cases have been recorded in Massachusetts through 1940; 14 others were recognized before 1930. Until 1934, no more than 15 cases were recorded in a single year, but since then the yearly report has been 40 or more cases. The principal reason for the increase is that physicians have become more alert in suspecting the disease. In Massachusetts, where the disease is largely due to Brucella abortus instead of to Brucella melitensis as it is in the Mediterranean countries, there is little tendency toward a seasonal predominance. In Malta persons of the two sexes are about equally affected, but in this country there has always been a predominance among males. In Massachusetts only 85 of the patients were female. Only 6 per cent of all the patients were less than 10 years of age and less than 11 per cent were between 10 and 19; in each decade thereafter the incidence is approximately double. Danger of infection in Massachusetts is not limited to any particular occupation. The disease is most prevalent in rural areas where pasteurization of milk is not the rule. As about 80 per cent of the population of the state lives in communities requiring pasteurization or certification of all milk sold, the incidence of the disease can be expected to be low.

New Jersey Medical Society Journal, Trenton

38:621-686 (Dec.) 1941

Technical Approach to Surgical Abdomen. R. S. Gamon, Camden.—p. 626.
*Sulfaguanidine: Absorption, Excretion and Therapy. C. A. Beling, Newark, and A. R. Abel, East Orange.—p. 629.
Unorthodox but Effective Treatment of Scarlatina. L. H. Rogers, Trenton.—p. 634.
Surgical Treatment of Hemorrhoids: New Method. H. E. Bacon, Philadelphia.—p. 636.
What Are Decibels? Painless Analysis. J. J. Roth, Newark.—p. 639.
*Treatment of Septic Thrombophlebitis with Heparin and Sulfathiazole. H. S. Davidson, Atlantic City.—p. 642.
Poliomyelitis in New Jersey. J. L. Mahaffey, Haddonfield.—p. 645.
Malarial Disease Uncovered by Autohemo Fever Therapy After Thirty-Five Years. T. P. Prout and Camella A. Losada, Summit.—p. 647.

Sulfaguanidine.—Beling and Abel determined the absorption and excretion of single and multiple doses of sulfaguanidine by giving 7 apparently normal persons a single dose of 3 Gm. at 8 a. m. and 10 adults 3 Gm. of the drug every eight hours for six to fourteen days. Venous blood was withdrawn after two, four and ten hours and, for four days, at 9 a. m. Examinations of the urine and the stool were made daily on pooled twenty-four hour collections. Excretion of sulfaguanidine in terms of the total ingested dose ranged from 29 to 66 per cent, with the exception of the excretion of 1 subject, which was 96 per cent. The excretion was less when multiple doses were given. Microscopic sections of the kidneys of rabbits given the drug and then killed did not reveal any deposition of crystals or damage to the glomeruli or tubules. Other organs appeared normal. The drug was effective in reducing the number of colon bacilli in the stools if concentrations of the total drug amounted to at least 1,000 mg. per hundred cubic centimeters for six to nine days. Higher concentrations may produce the same results within a shorter time. Streptococcus fecalis and the alpha streptococcus were effectively reduced in some cases. The anaerobic bacteria were not always influenced. Although the determination of the blood level is essential to check the absorption and the efficiency of renal excretion, this level was not necessarily correlated with or

indicative of the level in the stool. Three patients with ulcerative colitis were improved by sulfaguanidine therapy and 9 were not improved. Two patients undergoing operation on the colon did extremely well during their postoperative course. This may have been due to the preoperative and postoperative reduction of the number of colon bacilli in the stools. Crystals were found in the urine of all patients. The renal output was not diminished.

Heparin and Sulfathiazole for Septic Thrombophlebitis.—With the thought that giving heparin in septic thrombophlebitis would prevent the further extension of thrombosis, that the existing thrombus would become attached to the wall of the vein and that complicating embolism might not occur, Davidson administered heparin by vein continuously for nine days to a patient with the condition. There was no objection to the use of heparin, as it was not fibrolytic and would not liquefy the existing thrombus but would keep more thrombi from piling up. As the patient's blood on culture was positive for nonhemolytic streptococci, sulfanilamide and then sulfathiazole were given to sterilize the blood stream. No local venous thrombosis was encountered from the injection. Heparin was administered in physiologic solution of sodium chloride. The clotting time was tested at the bedside night and morning, and enough heparin was added to the infusion to keep the clotting time between fifteen and twenty minutes. At no time was there any edema or cardiac decompensation. Two cases are reported by the author which illustrate the prophylactic value of heparin and sulfathiazole in patients in whom peripheral thrombophlebitis is recognized. In his 2 patients fever was present, but blood cultures were sterile. Heparin therapy was instituted to render the blood less coagulable and to prevent the thrombus from extending. Sulfathiazole was given for its bacteriostatic action and to sterilize the blood stream and abolish possible embolic accidents. Both patients recovered.

New York State Journal of Medicine, New York

42:1-96 (Jan. 1) 1942

Direct Supravesical Extraperitoneal Cesarean Section. R. J. Pieri and F. R. Irving, Syracuse, N. Y.—p. 25.
*Plea for Earlier Diagnosis of Rectal Cancer: Analysis of 108 Clinic Patients. R. R. Braund and G. E. Binkley, New York.—p. 33.
Knott Technic of Ultraviolet Blood Irradiation in Acute Pyogenic Infections: Study of 103 Cases with Clinical Observations on Effects of New Therapeutic Agent. G. Miley, Philadelphia.—p. 38.
Practical Management of Eczema in Infants and Children. E. D. Osborne, J. W. Jordon and J. J. Hallett, Buffalo.—p. 47.
Adequate Treatment of Prostatic Disease, with Special Reference to Pathology. R. B. Henline, New York.—p. 51.
*Observations on Continuous Spinal Anesthesia. G. E. Burford and W. H. Galvin, New York.—p. 54.
Experience with Sulfapyridine and Sulfathiazole. W. D. Province and F. K. Heath, New York.—p. 59.
The Ideal Nose. A. A. Cinelli, New York.—p. 64.

Earlier Diagnosis of Rectal Cancer.—Braund and Binkley state that early diagnosis has not kept up with the progress made in the treatment of rectal cancer during the last twenty-five years. The early symptoms of rectal cancer are difficult to record, but an early manifestation of the disease may be any mild symptom that is sufficient to attract the patient's attention to the rectal region. Among 108 unselected patients observed by the authors the first recognizable symptoms were, in order of frequency, blood in the stool, constipation, increase in flatus, diarrhea, pain and mucus in the stool. The 108 patients sought medical advice on an average of eight and nine-tenths months after the onset of symptoms attributable to the rectal cancer. Of 100 patients referred the disease was diagnosed without undue delay in 25. They were referred within one month. For 75 there was an additional average delay of nine and nine-tenths months. During this delay the patients received inadequate or improper therapy. Twenty had not had a rectal examination, and 37 had had a digital examination which would have been sufficient for a tentative diagnosis if it had been performed properly. More than 90 per cent of the rectal cancers were within reach of the examining finger. Forty-six of the 100 referred patients saw two to five physicians before being referred to the clinic. This shopping around is evidence of the patients' dissatisfaction with and failure to improve under the prescribed treatment.

Spinal Anesthesia.—According to Burford and Galvin, the technic described by Lemmon for repeated injections of a small amount of an anesthetic drug into the subarachnoid space during an operation removes the possibility of an initial large injection proving toxic. The frequent small additions allow gradual detoxification. For the first time the headward diffusion of the anesthetic to the level necessary to produce adequate anesthesia can be approximately controlled. The short acting drug increases the safety of spinal anesthesia with this technic by rapidly losing effectiveness should too high a level of anesthesia become established. For the present, procaine hydrochloride is the drug of choice. Increased safety and reliability are the two major improvements. Theoretical disadvantages relate to the increased possibility of injury to nerve roots, to infection and to meningeal irritation. Minor complications have increased with the technic. The incidence of headache has increased by 10 per cent. The minimum of special equipment is (1) a malleable spinal needle, (2) fine bore, nonkinking rubber tubing and (3) a single Luer-Lok connection adapted to fit the spinal needle on one side and the fine bore tubing on the other.

Northwest Medicine, Seattle

40:435-478 (Dec.) 1941

Differential Diagnosis and Treatment of Jaundice. H. J. Tumen, Philadelphia.—p. 437.
Epidemiology of Poliomyelitis: Newer Developments. L. E. Powers, Tacoma, Wash.—p. 446.
Pathology of Poliomyelitis. C. P. Larson, Tacoma, Wash.—p. 448.
Neurologic Aspects of Poliomyelitis. R. W. Brown, Fort Steilacoom, Wash.—p. 450.
Treatment of Poliomyelitis. N. E. Magnussen, Tacoma, Wash.—p. 452.
Diabetes: Disturbance in Endocrine Regulation of Blood Sugar. S. Soskin, Chicago.—p. 457.
Stilbestrol in Treatment of the Menopause. C. D. Kimball, Seattle.—p. 464.
*Zinc Poisoning. T. E. P. Gocher, San Francisco.—p. 467.

Zinc Poisoning.—Gocher enumerates the complaints that follow exposure to the fumes and dust of zinc oxide, chromate, sulfate and chloride. They are dermatitis of the trunk and of the upper parts of the thighs, conjunctivitis, chills, gastrointestinal upsets, chronic anemia after about six months of exposure, boils and eczema. Abdominal influenza may cause an increase in the number of stippled erythrocytes, but this returns to normal as soon as the disease is cured. Abdominal cramps were not encountered if chills were not present. The average blood differential counts of 26 persons exposed to zinc were hemoglobin 85 per cent, leukocytes 8,000, polymorphonuclears 48 per cent, large lymphocytes 32 per cent, small lymphocytes 10 per cent, eosinophils 4 per cent, basophils 0 per cent, large monocytes 4 per cent, erythrocytes normal and about one stippled cell to about 2,000 erythrocytes. The dermatitis was usually a red, papular type that itched severely. It often disappeared spontaneously in two or three months with no recurrence. The rash was often associated with inflammation of the hair follicles. The 26 patients treated and cured were cured more readily if they were no longer in contact with zinc fumes or dust. The best prophylaxis for zinc absorption is good personal and plant hygiene and the use of proper respirators. No permanent disabilities were observed, but a certain number of men retained a distinct susceptibility and allergy to zinc salts.

Ohio State Medical Journal, Columbus

38:1-100 (Jan.) 1942

Urologic Diagnosis in General Practice. V. C. Laughlin, Cleveland.—p. 17.
Nutrition in National Defense Program. Martha Koehne, Columbus.—p. 24.
Clinical and Laboratory Diagnosis of Leptospirosis. Clara Raven, Youngstown.—p. 29.
Heterophile and Oral Pneumococcic Antigenic Action of Cold Vaccine. H. M. Powell, Indianapolis.—p. 32.
Treatment of Impetigo Contagiosa. M. T. Ebner, Cleveland.—p. 35.
Mattress and Pillow Coverings. H. Iker, Chicago.—p. 37.
What Shall We Do for the Pregnant Woman with Syphilis? L. J. Roth, Columbus.—p. 39.
Diagnostic Hints in Endocrinology. E. Podolsky, Brooklyn, N. Y.—p. 42.
Stilbestrol Therapy. E. E. Beard, Cleveland, and P. L. Rossman, Fort Wayne, Ind.—p. 43.
Consideration of Diseases of Blood Vessels in Diabetes Mellitus. M. H. Rosenblum, Steubenville.—p. 46.
Farmacias, Apothekes and Chemist Shops. H. Dittrick, Cleveland.—p. 50.
Unexpected Death in Young Individual with Cardiovascular Syphilis: Case Record Presenting Clinical Problems. S. Koletsky, Cleveland.—p. 54.

Pennsylvania Medical Journal, Harrisburg

45:193-320 (Dec.) 1941

Problems of Aging. E. J. Stieglitz, Bethesda, Md.—p. 211.
*Indications for Tonsillectomy. G. M. Coates and W. Gordon, Philadelphia.—p. 218.
Evaluation of Cryotherapy in Treatment of Post Acne Scars. L. Hollander, Pittsburgh, and J. M. Shelton, Washington.—p. 226.
*Endocrine Manifestations in Diabetic Patients. J. A. Daugherty, Harrisburg.—p. 229.
Use of Silver Picrate in Sinus Infections: Report of 200 Cases. L. Felderman, Philadelphia.—p. 232.
Experience with Vinethene as Obstetric Anesthetic. W. F. Hartman, Lancaster.—p. 236.
Relationship Between Blood Cholesterol, Sugar Tolerance and Basal Metabolic Rate in Thyroid Disease. K. Y. Yardumian and N. M. Wall, Pittsburgh.—p. 239.

Indications for Tonsillectomy.—Coates and Gordon discuss the indications for tonsillectomy as determined by the conditions within, adjacent to and remote from the tonsils. The conditions within the tonsils to be considered when tonsillectomy is contemplated are repeated attacks of tonsillitis, abscesses, Vincent's infection, epidemic streptococcic sore throat and tuberculous, diphtheritic and hypertrophied tonsils. Simple inspection of the fauces and tonsils will often fail to reveal all the foregoing manifestations, and laboratory studies must be resorted to. Children who are allergic or who give a family history of allergy should never be operated on during the hay fever season lest bronchial allergy and/or nasal allergy be precipitated. Conditions adjacent to the tonsils that may require tonsillectomy are acute catarrhal and chronic suppurative otitis media, deafness of the middle ear, labyrinthitis and deafness of the inner ear, sinusitis, thyroid disease, laryngitis, pharyngitis, cervical adenitis, peritonsillar abscess, and ocular disease. The authors do not suggest that tonsillectomy will cure these diseases but advise the operation only when tonsillar sepsis can be proved. Some of the acute and chronic conditions remote from the tonsil that may be traceable to infected tonsils are endocarditis, peritonitis, pleuritis, pericarditis, arthritis, optic neuritis, thyroiditis, herpes zoster, chorea, myositis, bronchopneumonia, appendicitis, enteritis, conjunctivitis, nephritis, pyelitis, neuritis and osteomyelitis.

Endocrine Manifestations in Diabetic Patients.—Studying the histories of 425 diabetic patients Daugherty found that 64 showed evidence of endocrine dysfunction other than dysfunction of the pancreas. The ages of the 64 ranged from 2 to 72 years. The disturbances were attributable to the gonads, the thyroid and the pituitary, and 9 patients had hepatic disturbances which may have been of endocrine origin. A typical case of each endocrine disturbance is presented to show its relation to the diabetic state. Only 1 patient had hyperfunction of the pituitary body, and the diabetes of this patient was severe. In the 3 with hypofunction of the pituitary body the diabetes was also severe. In 12 patients with hyperthyroidism the severity of the diabetes was increased and difficult to control. Severe diabetes seemed to be the rule also in the 10 with hypothyroidism; thyroid extract aided in controlling the diabetes. There were gonadal disturbances in 38 females which definitely affected the course of the diabetes. Hypofunction seemed to aggravate the diabetic state.

Proc. of Staff Meet. of Mayo Clinic, Rochester, Minn.

16:801-816 (Dec. 17) 1942

Some Effects of Hyperventilation, with Special Reference to Aviation Medicine. R. F. Rushmer, W. M. Boothby and H. C. Hinshaw.—p. 801.
*Palindromic Rheumatism: "New," Oft-Recurring Disease of Joints (Arthritis, Periarthritis, Para-Arthritis) Apparently Producing No Articular Residues: Report of Thirty-Four Cases (Its Relationship to "Angioneural Arthrosis," "Allergic Rheumatism" and Rheumatoid Arthritis). P. S. Hench and E. F. Rosenberg.—p. 808.

Palindromic Rheumatism.—Hench and Rosenberg describe a new entity, an arthritic recurring disease of joints and adjacent tissue characterized by multiple afebrile attacks of acute arthritis and periarthritis, sometimes also para-arthritis, with pain, swelling, redness and disability. Generally only one small or large joint is affected. The attacks appear suddenly, last for a few hours to one to three days and disappear completely, only to recur at short or long irregular intervals. Despite the transitory presence of an acute or subacute inflammatory polymorphonuclear exudate in the articular tissue and cavity there is little or no constitutional reaction or abnormality in laboratory tests, and no significant functional, pathologic or roentgen residues occur even after the disease has been present for years. Of the authors' 34 patients 19 were female and 15 male between 13 and 68 years of age; 70 per cent were between 20 and 39. The disease before admission had lasted from one year to twenty-five years. The frequency of attacks varied from two to ten a year to almost daily attacks in a few patients. In 90 per cent of the patients an attack was usually monarticular. Generally there was a relative lymphocytosis (the lymphocytes numbering 37 to 48 per cent) during or between attacks. Laboratory tests generally gave normal results, except that blood fats and total lipids were moderately elevated, suggesting some metabolic disturbance. Features favoring an allergic and an infectious origin of the disorder were present. A follow-up study of 27 patients reveals that the various types of treatment tried were ineffective. A cure which may have been spontaneous has occurred in 4, 12 have improved slightly in that their attacks are shorter or occur less often, the disease remains unchanged in 7, and 3 patients are somewhat worse in that they have attacks more often; 1 patient died of coronary disease.

Public Health Reports, Washington, D. C.

56:2365-2404 (Dec. 12) 1941

Child Health and Selective Service Physical Standards. A. Ciocco, H. Klein and Carroll E. Palmer.—p. 2365.
Industrial Injuries Among Urban Population as Recorded in National Health Survey. Joan Klebba.—p. 2375.

56:2405-2444 (Dec. 19) 1941

Quantitative Studies of Tuberculin Reaction: II. Efficiency of Quantitative Patch Test in Detecting Reactors to Low Doses of Tuberculin. M. L. Furcolow and E. L. Robinson.—p. 2405.
*Studies of Acute Diarrheal Diseases: V. Outbreak Due to Salmonella Typhi Murium. W. E. Mosher Jr., S. M. Wheeler, H. L. Chant and A. V. Hardy.—p. 2415.
Relapsing Fever: Ornithodoros Parkeri a Vector in California. G. E. Davis, H. L. Wynns and M. Dorthy Beck.—p. 2426.
Disabling Morbidity Among Industrial Workers, Third Quarter of 1941. W. M. Gafafer.—p. 2428.

56:2445-2484 (Dec. 26) 1941

Studies of Sewage Purification: XV. Effective Bacteria in Purification by Trickling Filters. C. T. Butterfield and Elsie Wattie.—p. 2445.
Ornithodoros Parkeri and Relapsing Fever Spirochetes in Utah. G. E. Davis.—p. 2464.

57:1-32 (Jan. 2) 1942

Indians and Selective Service. J. R. McGibony.—p. 1.
Coding and Tabulation of Medical and Research Data for Statistical Analysis. T. I. Edwards.—p. 7.

Acute Diarrheal Diseases.—Mosher and his colleagues discuss the occurrence of Salmonella typhi murium dysentery in 237 mentally defective persons and a matron. With the exception of that of the matron the infection was limited to inmates of twelve cottages served by a common kitchen. The diagnosis of the disease in 86 was established by the isolation of the organism; 2 passive carriers were discovered. In contrast to the Salmonella infection, which was acute, Shigella dysenteriae (Flexner and Sonne) was isolated frequently from persons with no evidence of previous symptoms. The Shigella infection in this institution, with the exception of one small outbreak, had previously spread slowly through the cottages and successfully maintained itself for several months. The available evidence indicates that the Salmonella infection was spread during Thanksgiving dinner through turkey or its dressing. This opinion was further supported by the fact that 3 inmates ate in the suspected dining room only on Thanksgiving Day and that the matron sampled the inmates' food. Repeated examination of 195 patients showed that 1 patient carried the organism for eighteen weeks. The primary source of infection may have been a carrier or a patient, contamination of food by rats or mice or a S. typhi murium infection contracted by the turkeys before they were killed. The human element does not seem probable. Cultural studies on rats trapped near the service building were negative, but they do not entirely exclude rodent contamination of the ingredients of the turkey dressing, especially the bread crumbs. However, the general cleanliness and order in the kitchen tend to obviate this probability. The original flock from which the probably incriminated batch of turkeys came could not be determined. The thermal death point for S. typhi murium is thirty minutes at 60 C. Nevertheless, in this outbreak the

organism apparently survived such a temperature. Turkey dressing is a good insulator against heat, and organisms deep in this dressing may have been stimulated rather than inhibited in their growth by the temperature of the oven. The second likelihood is that a septic infection with Salmonella was lodged in the deep tissues (marrow) of the turkeys and was comparatively inaccessible to heat.

Radiology, Syracuse, N. Y.

37:659-788 (Dec.) 1941

Nasal Sinusitis. G. W. Grier, Pittsburgh.—p. 659.
*High Voltage Roentgen Irradiation of Accessible Cancer of Skin and Mucous Membrane. G. P. Sims, Columbus, Ohio.—p. 666.
Physical and Biologic Considerations in Use of Slow Neutrons for Cancer Therapy. P. A. Zahl and F. S. Cooper, New York.—p. 673.
*Tracer Studies with Radioactive Phosphorus in Malignant Neoplastic Disease. J. M. Kenney, L. D. Marinelli and Helen Q. Woodard, New York.—p. 683.
Absorption of Radiophosphorus in Irradiated and Nonirradiated Mice. L. D. Marinelli and J. M. Kenney, New York.—p. 691.
Elimination of Radioactive Elements by Patients and Rabbits After Injection of Thorotrast. W. Stenstrom, Minneapolis.—p. 698.
Further Studies on Effects of Irradiation on Proliferation and Metabolic Processes of Normal and Malignant Mammalian Tissues: V. Effects Produced by Different Dosage Rates of X-Radiation on Growth Factors of Mouse Sarcoma 180 Grown in Vivo Following Irradiation in Vitro. Anna Goldfeder, New York.—p. 705.
Depth Dosage Measurements by Means of Goldfish. F. Ellinger and R. Gross, New York.—p. 717.
Biologic Effect of Roentgen Rays of Long and Short Wavelength on Totally Irradiated Rat. J. C. Potter, Rochester, N. Y.—p. 724.
Some Important Considerations of Soft Tissue Anatomy as Revealed by Radiography of Anatomic Cross Sections. J. R. Carty, New York.—p. 726.
Rectal Dyschezia: Misnomer for Megarectum. P. J. Delano, F. J. Ronayne and T. B. Boland, Chicago.—p. 730.
Parasternal Diaphragmatic Hernia: Report of Case on Right Side. R. A. Colmers, New York.—p. 733.
Portable Dark Room for Processing X-Ray Films Rapidly. C. Jones, Santa Barbara, Calif.—p. 740.
Study of Secondary Screening. G. Schönander, Stockholm, Sweden.—p. 743.

High Voltage Irradiation of Accessible Cancer.—Sims has obtained better results in treating many advanced malignant cutaneous lesions with high voltage roentgen therapy (200 kilovolts with medium filtration) than with low voltage therapy. Recurrences have been less frequent, the reaction to irradiation has not been so great, the tumor has regressed more rapidly and primary healing has occurred with less scarring. The total dose should depend on the response of the neoplasm and the reaction of the adjacent normal tissue. Fractionated treatment permits one to evaluate the dose better and to prevent undesirable reactions. So far no perceptible ill effects in the deeper structures have been encountered. The author does not believe that there is any selective action in different types of tissue with different qualities of radiation but believes that the quality produced by 200 kilovolts with heavier filtration gives a more homogeneous and more effective depth dose. The difference between the lethal dose for tumorous tissue and that for normal surrounding tissue appears to be greater with roentgen rays of shorter wavelength.

Radioactive Phosphorus in Neoplastic Disease.—To determine whether the isotope of radioactive phosphorus would be of value in the treatment of certain malignant neoplasms, Kenney and his associates administered about 0.5 microcurie of this isotope in the form of a 1.5 to 3 per cent solution at varying times before operation to patients with carcinoma of the breast, osteogenic sarcoma and lymphosarcoma. Measurement of the radioactivity of portions of the different tissues removed at operation suggests that radioactive phosphorus may be a useful therapeutic agent in lymphosarcoma and a valuable therapeutic adjunct in the treatment of osteogenic sarcoma and mammary carcinoma. As radioactive phosphorus is administered orally or parenterally and is distributed throughout the body it produces in fact a systemic irradiation. Its localization in tissue, as far as is known, is purely a metabolic phenomenon and is dictated by the metabolic need of tissue for phosphorus. Hence its effectiveness depends on its distribution in the body. If it should prove more effective than conventional radiation therapy, it will be so because of this, and especially so if there is a favorable differential absorption by scattered tumor cells.

Review of Gastroenterology, New York

8:421-506 (Nov.-Dec.) 1941

Some Aspects of Medical Treatment of Peptic Ulcer. F. D. Adams, Boston.—p. 421.
Surgical Aspects and Treatment of Peptic Ulcer. A. W. Allen, Boston.—p. 426.
*Nature of Functional Dyspepsia. F. J. Gregg and R. R. Snowden, Pittsburgh.—p. 432.
Diverticulosis: Analysis of Eighty-Six Cases. A. Levitt and K. Goldstein, Buffalo.—p. 439.
Gastrogenic Diarrhea. A. Bernstein, Chicago.—p. 447.
Comfortable Application of Nasogastric Tube. F. E. Barton, Boston.—p. 449.
*Cancer of Stomach in Children and Young Adults. H. I. Goldstein, Camden, N. J.—p. 450.
Cholesterol Ester Sol as Therapeutic Agent. E. L. Bortz and H. N. G. Kline, Philadelphia.—p. 458.
III. Studies of Liver Function of Normal and Diseased Livers from Bile Salt Concentration in Surgical Drainage Bile. L. M. Morrison and W. A. Swalm, Philadelphia.—p. 464.
Varied Clinical Aspects of Vitamin K Deficiency. H. A. Rafsky, New York.—p. 472.
Clinical Experience in Treatment of Acute Cholecystitis: Analysis of 100 Cases. H. Frankel, E. Abramson and J. E. Berk, Philadelphia.—p. 481.

Nature of Functional Dyspepsia.—Gregg and Snowden point out that an analysis of the records of 5,000 consecutive patients studied in the Pittsburgh Diagnostic Clinic shows that the complaints of 2,189 were referable to the gastrointestinal tract and warranted complete diagnostic studies. For 1,039, or 47 per cent of the 2,189, a diagnosis of functional dyspepsia was made. A study of the symptoms, physical signs and laboratory evidence presented by the patients with functional dyspepsia, as compared with the same factors in those in whom organic disease was present, shows that there is no characteristic group of symptoms or physical signs and that the ultimate diagnosis of a digestive disturbance should be based on a complete study not only of the intestinal tract but of the gallbladder.

Gastric Cancer.—Goldstein states that a review of the available medical literature of the world for the last hundred years reveals that there have been recorded approximately 350 cases of malignant growths of the gastrointestinal tract in infants, children and young (less than 26 years of age) adults.

Rocky Mountain Medical Journal, Denver

39:1-80 (Jan.) 1942

Medical Problems of Today. F. H. Lahey, Boston.—p. 19.
Use of Prostigmine-Morphine in Obstetrics. D. Slaughter, J. M. Siever and R. E. Martinak, Dallas, Texas.—p. 24.
Dysmenorrhea. R. J. Crossen, St. Louis.—p. 28.
Gastrointestinal Diagnosis. F. J. Hodges, Ann Arbor, Mich.—p. 33.
Use of Posture to Secure Unilateral Intensification of Spinal Anesthesia. R. P. Middleton and A. W. Middleton, Salt Lake City.—p. 36.
Aniseikonia. V. H. Brobeck, Colorado Springs, Colo.—p. 38.
Manifestations and Management of Asthma. W. C. Service, Colorado Springs, Colo.—p. 41.

South Carolina Medical Assn. Journal, Florence

37:317-350 (Dec.) 1941

Sprue. H. Smith, Greenville.—p. 317.
*Tick Paralysis in South Carolina. M. W. Beach and B. O. Ravenel, Charleston.—p. 323.
Recognition and Treatment of Common Painful Back Disorders. W. R. Mead, Florence.—p. 325.

Tick Paralysis.—Beach and Ravenel report an instance of tick paralysis caused by Dermacentor variabilis. A child of 4 became sick the morning prior to admission to the hospital and had weakness, general malaise, difficulty in arising and a staggering gait. These complaints ceased after an hour, and the child played the rest of the day. On the morning of admission the patient had headache and weakness of the lower extremities on walking. The child was hospitalized. Her condition remained about the same until the second day. While combing the patient's hair a nurse discovered a partially engorged tick. The tick was identified as a female Dermacentor variabilis. Further search did not reveal more ticks. The child's symptoms cleared rapidly, and on discharge twelve days later there was no muscular weakness and only a slight ataxia. The patient was seen two weeks later, and she appeared completely recovered.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2:717-758 (Nov. 22) 1941

*Combined Active and Passive Immunization Against Diphtheria: I. Studies of Antitoxin Response in Normal Students. A. W. Downie, A. T. Glenny, H. J. Parish, W. Smith and G. S. Wilson.—p. 717.

Pneumococcic Peritonitis: Four Cases. C. Noon.—p. 724.

Cutaneous Anthrax Treated by Arsenicals and Sulfapyridine. I. M. Davidson.—p. 725.

Dark Adaptation and Miners' Nystagmus. I. Campbell.—p. 726.

Active and Passive Immunization Against Diphtheria.—Downie and his collaborators attempted to select a dose of toxoid small enough to reveal any inhibitory action of the serum, a dose of serum that would not conceal the active formation of antitoxin in the body following the injection of toxoid and a toxoid that would not interfere with the action of serum. Studies were carried out on third year medical students aged between 20 and 22 and on some boys, all but 2 of whom were between 14 and 19, at a training colony. The subjects were Schick tested. From 6 to 8 cc. of blood was withdrawn from those giving a positive reaction, and the blood was titrated for diphtheria antitoxin. The subjects giving positive reactions were divided into A and A + P groups. The 148 subjects in group A (active immunization) received 0.1 cc. (5 Lf) of alum precipitated toxoid, and the 131 in group A + P (active plus passive immunization) received 0.1 cc. of alum precipitated toxoid and 350 to 500 units of refined diphtheria antitoxin. All injections were subcutaneous. Four weeks later blood was withdrawn and the subjects were given 0.3 cc. of alum precipitated toxoid. Eight weeks after the second dose, blood was withdrawn, the subjects were Schick tested and those having a positive reaction were given 0.3 cc. of alum precipitated toxoid. The results show that the simultaneous administration of antitoxic serum and alum precipitated toxoid delays and slightly inhibits the formation of fresh antitoxin. With a few exceptions the average antitoxin content of the serum of the A + P group fell from about $\frac{1}{50}$ unit one week to between $\frac{1}{500}$ and $\frac{1}{1,000}$ unit per cubic centimeter of blood four weeks after the first injection. The Schick conversion rate eight to twelve weeks after the second dose of alum precipitated toxoid was 95.7 per cent for the A and 90.5 per cent for the A + P group. The dose of alum precipitated toxoid was so small that most of it was neutralized by the simultaneously injected serum. Therefore a larger dose of alum precipitated toxoid given at the first injection to A + P subjects might cause a higher degree of sensitization and decrease or abolish the difference in the rate and the amount of antitoxin produced by A and A + P subjects. If the same sort of intermediate stage of relative susceptibility between the disappearance of passive and the development of active immunity appears in man as has been observed in guinea pigs, the injection of serum with the first dose of alum precipitated toxoid may not have any advantage over ordinary active immunization.

Lancet, London

2:625-656 (Nov. 22) 1941

Common Sulfonamides: Nomenclature, Structure and Uses. D. G. Ardley.—p. 625.

Active Immunization Against Tetanus. D. G. Evans.—p. 628.

*Placental Blood in Treatment of Amenorrhea. J. Halbrecht.—p. 630.

*Meningococcic Infection. R. C. Dickson, D. Magner, N. E. McKinnon and N. B. McGillivray.—p. 631.

Paradoxic Cerebral Embolism with Recovery. A. G. Porter.—p. 634.

Isoagglutinin Changes After Transfusion of Incompatible Blood and Serum. P. L. Mollison and I. Maureen Young.—p. 635.

Stab Wounds of Heart and Pericardium: Four Cases with Three Recoveries. T. Schrire.—p. 638.

Placental Blood in Treatment of Amenorrhea.—Halbrecht studied the effect of the injection of the plasma of placental blood in 34 women with amenorrhea and sterility. Eighteen of them menstruated within five to thirty-five days after the end of a course of treatment. Three other patients menstruated on or after the thirty-fifth day. The effect of the plasma of placental blood on the uterine mucosa of 11 women was determined by microscopic examination before and after treatment, which consisted of five or six injections of 150 to 200 cc. of the plasma. Treatment was ambulatory, and the interval between injections was usually one day. The endometrium before treatment was more or less atrophic. After three injections 5 patients showed a complete change from atrophy to the proliferative or secretory state. All 5 menstruated shortly after treatment, although they had been amenorrheic for five months to two years. Another patient menstruated twenty days after the beginning of treatment, but the mucosa remained atrophic. The endometrium of the other 5 patients did not react. The one remaining ovary of 1 of these women had been removed a year before. This suggests that the action of placental blood depends not on its content of estrogenic substance but on the gonadotropic substances present in it. The 5 unresponsive women had not menstruated for two to fifteen years and had an early climacterium. In the women who menstruated or showed changes in the endometrium the size of the uterine cavity increased from 1 to 2.5 cm. Follow-up study of 13 of the 18 women who menstruated after treatment revealed that 5 did so only once and 8 two or more times.

Meningococcic Infection.—Dickson and his co-workers observed 26 patients with meningococcic infection between July 1940 and July 1941. Of these 11 did not have meningitis on admission (though it subsequently developed in 1) but had meningitis septicemia. The infection was sporadic, occurring in every month of the year, and came from Canadian troops stationed in England. Nine of the 11 patients without meningitis were treated with sulfapyridine during the ameningitic phase; 8 recovered completely after 34 Gm. of the drug had been administered in seven days; 12 Gm. was given in the first twenty-four hours. For 1 patient the diagnosis was not made and treatment was not instituted until the disease had been present for three months. The infection was cured by chemotherapy, but there was residual articular pain. The remaining 2 men were not given sulfapyridine until meningitis developed. In 1 case the diagnosis was missed because several blood samples did not show any growth. Such evidence is evidently inadequate to exclude the diagnosis when diagnostic clinical signs are present. This patient made an apparently spontaneous recovery, was free of recurrence three months later but was invalided home because of residual articular pain. The histories of the patients revealed that while the beginning of meningeal inflammation cannot be determined precisely the evidence suggests that it begins about the time that severe persistent headache ensues. Such a headache was never the first symptom. Eight of the 9 patients in whom the premeningitic period lasted more than one day gave a history of localized articular pain, associated with localized muscular pain in 6 and with cutaneous lesions in 5. The 5 with a premeningitic period of more than a week gave a history of remissions and relapses. In 3 of the 6 in whom the premeningitic period was less than one day the symptoms were similar to those of the patients without meningitis. In addition to the usual symptomatic treatment, sulfapyridine was used as for the ameningitic patients but was continued for ten days, and a total of 40 Gm. was given. The dose by mouth was usually augmented by the intravenous administration of 2 to 4 Gm. of sulfapyridine sodium at the onset of treatment. Of the 16 patients, 12 made a rapid and complete recovery in three to five days, 2 are still ill and 2 died. There is no reason to suppose that a peculiar susceptibility or resistance of the host was operative in this series. Organisms of several different agglutinative types were recovered, and their difference apparently excludes the possibility that a special characteristic of the organism was important in determining the course of the infection.

Tubercle, London

22:231-256 (Oct.) 1941

Bronchial Obstruction in Pulmonary Tuberculosis. P. R. Allison.—p. 231.

Diagnostic and Prognostic Value of Estimations of Free Sugar in Pleural Effusions. E. Nassau.—p. 249.

Schweizerische medizinische Wochenschrift, Basel

71:1193-1228 (Oct. 18) 1941. **Partial Index**

Therapy of Parenchymal Diseases of Liver. W. Nonnenbruch.—p. 1193.
Action of Ephedrine in Myasthenia Gravis. J. H. Burn.—p. 1196.
*Practical Experience with Depot Therapy of Adrenal Insufficiency. S. Thaddea.—p. 1202.
Recidivations of Infantile Acrodynia. M. Péhu.—p. 1207.
Therapy with Organic Phosphorus Preparations. E. Bürgi.—p. 1209.
*Therapy of So-Called Idiopathic Spontaneous Pneumothorax. A. Brunner.—p. 1210.
Therapy of Ménière's Vertigo. E. Lüscher.—p. 1218.
*Therapy of Scabies with Benzyl Benzoate. W. Lutz.—p. 1224.

Depot Therapy of Adrenal Insufficiency.—At Thaddea's clinic 7 patients with Addison's disease were treated by subcutaneous implantation of desoxycorticosterone acetate. Best results were obtained when from 100 to 200 mg. of the substance was implanted. The improvement of the adrenal insufficiency which follows the depot therapy persists for three to six months. It not only becomes manifest in the subjective condition of the patients but can be demonstrated by objective functional tests. A noteworthy advantage of this form of treatment is the considerable saving of the crystalline substance. The author concludes that the depot treatment with desoxycorticosterone acetate is a valuable addition to the therapeutic armamentarium in chronic adrenal insufficiency.

Treatment of Idiopathic Spontaneous Pneumothorax.—According to Brunner, spontaneous pneumothorax is not always of tuberculous origin but may be caused by the rupture of emphysema blebs. Nontuberculous spontaneous pneumothorax may be mistaken for cardiac disorders or emphysema; it may become manifest in a gradually increasing dyspnea. The fact that the author observed 3 cases in three months indicates that it is not as rare as is assumed. If the excess pressure threatens the patient's life it must be immediately counteracted. Relieving the pressure frequently permits the lung to reexpand to such an extent that it adheres to the thoracic wall and closes the pulmonary fistula. If the pneumothorax shows no tendency to decrease or if it increases in spite of repeated removal of air the aim of the treatment is to close the pulmonary fistula. In cases of tension pneumothorax the author uses valvular drainage. In cases of spontaneous pneumothorax not accompanied by severe dyspnea pneumothorax must be corrected so that respiration is facilitated and escape of air from the lung is prevented. This requires control of the pressure in the thorax by means of a pneumothorax apparatus. In many cases spontaneous pneumothorax heals in a short time under this treatment; in others the pulmonary fistula closes spontaneously. Pulmonary fistulas with wide openings require prolonged suction drainage.

Therapy of Scabies with Benzyl Benzoate.—The benzyl benzoate method of treating scabies was introduced by Nielsen of Copenhagen in 1912. Lutz employs a mixture of 300 parts of benzyl benzoate and 600 parts of spiritus saponis Hebrae. This mixture is more homogeneous and adheres to the body better than did the original mixture. Lutz employed it with satisfactory results in 160 cases. There were no relapses, as was sometimes the case with the old soft soap-sulfur treatment. Itching subsides at once. Application is more rapid and simple than with the soap-sulfur method. The disadvantage of the method is that it causes a burning sensation of the skin. This can be lessened by giving the preliminary soft soap bath, according to Kissmeyer's simple method rather than with a previous application of soap, ten minutes' waiting and brushing in the bath.

Hospital, Rio de Janeiro

20:855-998 (Dec.) 1941. **Partial Index**

Riboflavin and Pyridoxine in the Tuber of Dioscorea Brasiliensis-Willd. C. Camargo Nogueira and F. A. de Moura Campos.—p. 855.
*Histamine in Therapy of Ménière's Disease. A. Monteiro.—p. 865.

Histamine in Therapy of Ménière's Disease.—Monteiro reports the case of a woman aged 38 who for many years had typical Ménière's disease. The patient was allergic, and there were allergic members in the family. Administration of quinine and estrogen in large doses failed to relieve the symptoms. She was given an intradermal injection of histamine solution in a dose of 0.25 mg. every four days for six doses. The patient apparently was cured. Discontinuation of the therapy resulted in recurrence of the symptoms. Administration of a new series of twelve histamine intradermal injections again controlled the symptoms. The author believes that Ménière's disease is an allergy to organic histamine. The intradermal injection of small doses of histamine produce desensitization of the patient through which the allergy is controlled.

Pediatria Prática, São Paulo

12:233-294 (July-Aug.) 1941

*Roentgenologic Diagnosis of Acute Pulmonary Disorders and Their Complications in Children. A. Pires de Campos and A. Delmanto.—p. 233.
*Encephalitis Following Measles. G. de Mattos and P. Refinetti.—p. 255.

Roentgenologic Diagnosis of Acute Pulmonary Disorders.—Infectious pleuropulmonary diseases of childhood produce extremely diverse clinical pictures. Meteorism and abdominal pain frequently are the initial symptoms. They are caused by intestinal hyperemia and by the central nervous reflexes so common in childhood. Pires de Campos and Delmanto present clinical histories of 12 children with acute pulmonary disease. One child presented signs of appendicitis, but careful examination disclosed a pneumonic focus in the right pulmonary apex. Hepatobiliary symptoms and neuralgic pains in the scapulohumeral region were other early symptoms of acute pulmonary disease. The authors emphasize the diagnostic importance of roentgenologic examination of the thorax in cases in which the symptoms are doubtful or difficult to interpret.

Encephalitis Following Measles.—Because of its comparative rarity, de Mattos and Refinetti report 2 cases of encephalitis following measles. The first patient was a boy aged 4 who had diffuse encephalomyelitic symptoms, optic neuritis and blindness. The general condition was greatly improved a month after the onset of the disease, and the neurologic symptoms had nearly all disappeared, except for the blindness. The second patient was a girl aged 18 months who had symptoms of parkinsonism five days after an attack of measles. A permanent cure followed in the course of a month.

Acta Chirurgica Scandinavica, Stockholm

85:455-556 (Oct. 31) 1941. **Partial Index**

Late Death After Lightning Burns: Case. H. Sjövall.—p. 455.
Chemical and Roentgencrystallographic Studies on Concrements from Urinary Tract. A. T. Jensen.—p. 473.
Chondromatosis of Knee Joint. S. Radner.—p. 487.
Renal Cyst with Peculiar Concrement Formation: Case. P. Rudström.—p. 501.
*Cholesterosis of Gallbladder. O. Arnell.—p. 511.
Fractures of Neck of Radius in Children. A. Roosvall.—p. 540.

Cholesterosis of Gallbladder.—Arnell designates as cholesterosis of the gallbladder a condition which has been called strawberry gallbladder, fish-scale gallbladder and the like. The condition is comparatively frequent. His observations were made on 110 patients who underwent surgical treatment at his hospital. Disturbances of cholesterol metabolism are the chief causes. Infection of bile ducts does not seem to be of etiologic importance. Cholesterol deposits in themselves do not as a rule impair the function of the gallbladder, nor do they cause symptoms. In patients coming to operation the cause of the symptoms is not uniform. In some the thickened mucous membrane, at times with callosities between the neck and the cystic duct, may produce a mechanical obstruction to the outflow of bile through the cystic duct. This explains attacks of pain and roentgenograms with poor or negative contrast filling. In other cases anatomic anomalies, such as kinks in the cystic duct, excessive development of Heister's valve or abnormal mobility of the gallbladder, constitute the basis for symptoms with cholesterosis as a contributing cause. In a number of cases in which cholesterosis is slight it is secondary to biliary disturbances of variable origin. Complications, such as infection and gallstones, may arise. Cholesterosis may be the direct cause of gallstone formation, as in the type in which polyps are formed, but this is rare. Except for this type there is probably no relationship between gallstones and cholesterosis. With the exception of the polypoid type, in which roentgenologic examination clarifies the problem, a definite diagnosis is often impossible. Late results of surgical intervention for cholesterosis were the same as those seen after cholecystectomy for cholecystitis or cholelithiasis.

THE STUDENT SECTION

of the

Journal of the American Medical Association

Devoted to the Educational Interests and Welfare of Medical Students, Interns and Residents in Hospitals

SATURDAY, MARCH 21, 1942

Education in Industrial Health

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TEXARKANA, TEXAS

The President's program for the manufacture of 120,000 tanks, 185,000 planes, countless anti-aircraft guns, the addition of millions of workers to our labor forces and the increase by one half during the next year of industrial employment in manufacturing, mining, construction, transportation and utilities demonstrates that the war will be won or lost on the assembly lines. The industrial worker has been given a place of special prominence in the prosecution of war efforts. Loss of working time by skilled and indispensable workers, no matter what the cause, must be classed today as casualties. The importance of the mobilization of medical facilities in order to meet the impact of the problems which are arising has been recognized for several years. The necessity for the coordination of effort of various agencies interested in the health and medical care of the defense worker has been generally admitted, and real progress has been made in defining spheres of activity and bringing about the cooperative effort which is imperative for victory.

In any discussion of this subject the terms "industrial health," "industrial medicine" and "industrial hygiene" have a tendency to become confusing, and the need of clarification of terms used is obvious. The connotations of the words "occupational" and "industrial," in relation to disease, are evidence of the necessity of a careful analysis of terms used. Industrial medicine may be considered as a science which deals with prevention, cure and alleviation of disease as it affects gainfully employed individuals. The objectives of industrial medicine have been stated to be:

1. To fit every person to types and quantities of work according to his ability to perform such work continuously without undue impairment, without injury to himself or his fellow workmen, and with profit to himself and his employer.

2. To procure and maintain fitness for work through efforts applied to the worker as an individual.

3. To educate the worker to a comprehension of the value and significance of physical and mental well-being and, in particular, of personal hygiene and accident prevention.

4. To reduce all loss of time, absenteeism and short work spans in industry the cause of which may be related in any way to health.

This concept indicates that much of industrial medicine may be beyond the field of the average practitioner and makes apparent the fact that industrial medicine is, to a large extent, the practice of medical supervision, preventive medicine and public health within the confines of industry.

Industrial health as a field of special medical interest is relatively young. Its origin, early difficulties and subsequent development are well within the memory of many physicians today. Relatively few physicians gave serious attention to safe and healthful practice in industry thirty years ago. Few physicians realized the preventive character of most occupational disorders. The rapid development of industry which gave rise to constantly multiplying hazards was followed by a lag in the development of measures, both preventive and curative, to cope with this situation. The perfection of methods of treatment and of technics of prevention by physicians, hygienists and engineering specialists in this field has been followed also by a lag in their articulation with the rank and file of practicing physicians who care for the great mass of industrial workers. The lag which has occurred is due to two factors; one is the extremely rapid development of industry in this country and the other is the failure of medical educators to give proper emphasis to the training of students, both undergraduate and graduate, and to assign to preventive medicine the place which its importance justifies. The implications of the development of industry and the change in the practice of medicine effected by workmen's compensation laws have not been sufficiently emphasized.

Read before the Thirty-Eighth Annual Congress on Medical Education and Licensure, Chicago, Feb. 17, 1942.

Experienced physicians in industry have testified that industrial health activity falls into three principal categories:

1. Industrial medical administration.
2. Industrial medicine and traumatic surgery.
3. Industrial hygiene and toxicology.

For physicians who expect to meet the ordinary medical needs of industry, proper grounding in each of these major subdivisions should be provided beginning in the undergraduate curriculum.

Medical service to industry flows through three principal professional channels:

1. The private practitioner in general or special practice serving on call or part time. Best current estimates indicate that 80 to 85 per cent of medical service to industry is supplied in this fashion. About thirty-four million individuals are employed in the industrial plants of the country. Medical care has been mainly remedial in character, to such an extent that medium sized and small plants have been left without the considerable advantages of preventive industrial medicine and surgery.

2. The full time industrial physician serving in one or several plants who exemplifies specialty practice in industrial health. In addition to prevention and treatment of compensable disability, he is concerned with the details of medical department administration.

3. The medical industrial hygienist more frequently associated with governmental agencies who provides a consultative and investigative service directly to industry and to the medical profession, as well as enforcement of public health and sanitary codes relating to conditions of work.

In each of these classifications there are definite shortages of well trained personnel. With notable exceptions the requirements of industry in the fields of industrial medicine, surgery and hygiene are being met in very incomplete and fragmentary fashion, without clear realization of objectives or their value to the health status of the community as a whole. It is clear that the medical profession has been hampered in its approach to this useful and expanding professional activity and will continue to be hampered until adequate provision is made for instruction in modern industrial health methods, both before and after graduation. To meet these varying educational requirements, medical and professional schools and medical societies singly and in combination are under heavy obligation to create or improve opportunities for training in undergraduate and continuation courses and for extended graduate study.

Since its organization in 1938, the Council on Industrial Health has stressed the importance of the care of workers in small industries, in which it is estimated that 85 per cent of industrial workers are employed. It is the general belief that the hazards of industrial poisons are present chiefly in the large companies and seldom in the small ones. There is, however, good reason to believe that the individual worker in the small plant is exposed to more hazards or to the same hazards in more ways than the man in the large plant. A number of statistical studies indicate that absenteeism due to non-occupational accidents and diseases is greater in the small establishment than in the large. The complex problems surrounding the provision of industrial health service to this important segment of the working population has received the serious consideration of several groups. The practicing physician is one of the most important factors in the delivery of this care.

The interest of the Council in education in the industrial health field has been expressed in (1) the original report of the Committee on Scope, (2) the formation of a subcommittee on education in the Council, (3) articles on industrial medical education in the special Industrial Health issues of THE JOURNAL, (4) instructions to state and county committees and (5) the development of a syllabus for undergraduate and graduate teaching in medical schools.

The Council on Medical Education and Hospitals, after reviewing several recommendations from the Council on Industrial Health, has authorized the latter council to assume the initiative in calling to the attention of medical schools deficiencies in trained personnel for various phases of industrial practice. This council has prepared a syllabus for undergraduate and graduate levels and has reviewed the work in this field of a committee of the American Association of Industrial Physicians and Surgeons. The recommendations of the latter group are also ready for consideration.

The Council reviewed the four year medical curriculum in 1938 and found that fifty-two schools reporting averaged five hours of instruction in industrial health. A recent review by Wampler reports that fifty-one schools averaged six and seven-tenths hours, an increase in the three year period of approximately one and seven-tenths hours. Wampler's report shows that twenty schools have increased the number of hours devoted to industrial health in the past three years. In thirty-five schools, industrial health is made a part of the course in preventive medicine and public health. Schools not having special courses state that the subject is cared for in the teaching in various clinical and preclinical departments.

Actually, only a few medical schools have made adequate provision for this type of instruction. Industrial hygiene is widely taught as a

relatively minor function of preventive medicine and public health. Problems in industrial medicine and surgery are presented without any relation to prevention and control over exposures and only as examples happen to present themselves in clinics or wards. Industrial medical administration has been almost completely ignored. Yet the experience of a number of medical schools amply demonstrates that reasonable acquaintance with the whole subject can be provided at modest expense through judicious use of time and readily available teaching and clinical material. The all important requirement for improved instruction is a unified plan which assigns over-all responsibility for coordinated classroom discussion, field studies and laboratory and section work to one single teaching division, preferably preventive medicine and public health. There must always be considerable dependence on clinical teaching in the medical and surgical aspects of industrial practice, but the testimony of recent graduates clearly indicates that older methods of divided and unrelated instruction fail to provide dependable and reasonably complete information.

As a matter of fact, progress would be greatly accelerated if more medical and graduate schools, especially those in industrial areas, could develop or attract support for the organization of separate teaching divisions in industrial health, each with its own faculty, and develop affiliations for clinical and demonstration material and facilities for laboratory and field investigation and consultation. Good precedent exists for independent organization of this character. Under such an arrangement there should be greatly improved prospects for the attraction of special teaching talent and material and of support for research into numerous aspects of industrial health demanding investigation and for the promotion of advanced training at graduate and fellowship levels.

One attitude toward the teaching of industrial health in the undergraduate years is that this subject should be included in the teaching of various specialties and that it should not be taught as a separate course and in a special department. The same attitude has been maintained with respect to the teaching of public health and preventive medicine. It is the opinion of the Council on Industrial Health that instruction in industrial health should be carried out under a separately organized department and with a definitely outlined curriculum. The syllabus prepared by the Council and the outline of instruction prepared jointly by the Council and the Committee of the American Association of Industrial Physicians and Surgeons are available for consideration.

Discussions of the problems of undergraduate teaching of industrial health in the last few years have resulted in general agreement that medical schools have an opportunity, through this channel, to influence the lives of millions of workers. The important services which physicians render are four: conservation of health, the treatment and when possible the arrest of incipient disease, the restoration of the sick to health and the relief of suffering. The relative importance of these functions is not generally recognized and, were medical educators to give proper emphasis to the training of students in preventive medicine and public health, it might well constitute their most important contribution to the reduction of the cost of medical care.

"In his work Affections, Hippocrates says 'I may venture one more question: What occupation does he follow?' Though this question may be concerned with the existing causes yet I regard it as well timed or rather indispensable, and it should be particularly kept in mind when the patient to be treated belongs to the working people. In medical practice, however, I find that attention hardly ever is paid to this matter." This quotation, which has such a direct bearing on the problems which we are discussing today, was written over two centuries ago by Ramazzini. The present emergency should create, through education, opportunities for competent physicians in all industries, large and small, not solely as a contribution to the preparedness effort but as a continuing activity in the field of preventive medicine. In the past the health needs of industry have been supplied by a small group of full time practitioners and hygienists, almost all of whom have developed without formal training, and a vast group of private practitioners who have been interested in remedial and reconstructive action almost to the exclusion of prevention.

DO YOU KNOW WHAT PHYSICIAN—

1. Was a leading American neurologist, a trustee of the University of Pennsylvania and also a famous novelist and poet?

2. Compiled a general index to British and foreign literature known as Bibliotheca Britannica? *(The answers are on page 1022.)*

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

Northwestern on Accelerated Schedule—Blood Donors

Northwestern University Medical School, Chicago, has adopted the accelerated war schedule and is now to be in session throughout the year on a quarterly basis. Every nine months a new group of freshman students will enter. The first group starts late in the month of June, and a full quota of seniors will be graduated at equal intervals after completing about three years of constant study. It is inspiring, our correspondent writes, to realize how efficiently the members of the staff who did not leave with the Northwestern General Hospital unit have maintained adequate teaching. In addition to the classes in military and tropical medicine for juniors and seniors, chemical warfare is taught on Saturday afternoons to sophomores, juniors and seniors. At least 95 per cent of Northwestern medical students have donated a pint of blood to the American Red Cross under the plan adopted and organized by the interfraternity council. The total will be approximately 500 pints. The local air raid protection units which are being organized in Chicago as in other cities may include medical students. It is proposed that each medical fraternity form a team of older students so that men will always be at hand from each group to aid in transportation or dressing of the wounded. These changes in student life offer financial difficulties to many. However, the university has outlined a student loan policy whereby the student can make his way without a summer job.

New York University Student Loan Fund

The freshman class at New York University School of Medicine, New York, held a dance, February 14, attended by many of the faculty members and about one hundred couples. The proceeds were given to the Student Loan Fund. Another dance was given March 14 for the Student Loan Fund by the general student body. In view of the three year curriculum recently put into effect to aid in the war effort, the financial problems of many students who depend on summer work to aid them has become acute. The Student Loan Fund is making an extra effort to be in a position to aid as many students as possible.

Johns Hopkins

Most of the students at Johns Hopkins University Medical School, Baltimore, have subscribed to courses in first aid being given by the Johns Hopkins Hospital staff members, which will continue once a week in the evenings for fifteen weeks. A second course is given for the same length of time for instructors in first aid. Both courses are sponsored by the American Red Cross. A new gymnasium was opened on December 3, 1941. The gymnasium is open not only to students but to members of the faculty and hospital staff.

Annual Student Meeting

The section on medical history of the College of Physicians of Philadelphia held its annual student meeting on December 8 with the following program: Dr. Robert A. Groff, Historical Aspects of Neurosurgery; Stanford Mulholland, "Development of Modern Urology," and Isidor S. Ravdin, "Some Contributions of American Surgery to the Art and Science of Medicine."

Louisiana's February Commencement

The class at Louisiana State University School of Medicine which ordinarily would have graduated in June graduated February 18 and, according to the dean, Dr. B. I. Burns, is one of the first, if not the first, class to graduate in this country under the accelerated program. Of the eighty members of the class who were eligible for commission in the Army, Navy or Public Health Service, 81 per cent have applied for commissions. The commencement speaker was Dr. C. S. Boucher, chancellor of the University of Nebraska and formerly dean of the College of Arts, Literature and Science at the University of Chicago, and president of West Virginia University. The dean announced that F. E. McCarty had received the award in obstetrics and gynecology, George A. Degenshein the award in medicine, Dionisus V. Cacioppo the awards in surgery, pediatrics and urology, and that Walter M. Woodward was awarded the George S. Bel Memorial Prize.

Columbia University

During the academic year 1940-1941, there were one thousand one hundred and forty-four applicants for admission to the school of medicine of Columbia University, New York, for the coming year; in the first year class for the last academic year 110 students were enrolled. According to the report of the dean, the class graduated obtained internships in fifty-five different hospitals in all sections of the country; Theodore Gold was awarded the Janeway Prize given to the member who ranked highest in efficiency and ability; Paul A. Kirschner was given the William Perry Watson Prize for outstanding work in the study of the diseases of children; William Stone Jr. was awarded the Thomas F. Cock Prize for a thesis entitled "Studies of Inclusion Blennorrhea Virus in the Genitourinary Tract," and Clarence J. D'Alton was given the Harold Lee Meierhof award for "conspicuous effort in pathology." The employment office of the medical school helped two hundred and thirty-nine students to obtain steady positions and one hundred and sixteen to obtain temporary jobs, exclusive of thirty-two positions provided by the National Youth Administration. About 45 per cent of the student body seek employment while they are in medical school.

The medical school offered two hundred and thirty courses in its postgraduate program during the year, designed and attended by physicians in general practice. Many new courses in the postgraduate program were introduced during the year, with emphasis primarily on recent advances in methods of diagnosis and treatment and interpretation of diagnostic laboratory procedures. During the year nine hundred and eighty-eight physicians were registered for postgraduate study and, while most of them were from the New York metropolitan area, physicians from forty-three states, four territories and twenty foreign countries were in attendance. The increased enrolment of Latin-American physicians was indicative of the importance of the program in promoting exchange of mutual interest among the medical profession of the Western Hemisphere. At commencement there were awarded one hundred and four degrees of doctor of medicine, thirteen of doctor of medical science, twenty-two of master of science (public health) and fourteen of bachelor of science (nursing).

Pennsylvania Undergraduate Medical Association

The Undergraduate Medical Association at the University of Pennsylvania School of Medicine will hold its annual meeting for presentation of student research on April 9. All classes in the medical school will be suspended on this day in order that all may attend the meeting. The program will consist of three formal lectures and a number of student research papers. Awards will be made for the outstanding papers. At open meetings throughout the year the Undergraduate Medical Association presents speakers of special interest. On December 11 Dr. Russell Wilder of the National Research Council spoke on "Nutrition in National Defense," and on February 5 Capt. C. H. Stevensen of the Bureau of Medicine and Surgery of the United States Navy spoke on "Military Medical Observations in England." Dr. Louise Pearce of the Rockefeller Foundation at Princeton, N. J., will address the annual open meeting of the Women's Medical Society on April 10. She will speak on some phase of the work in experimental syphilis.

Louisiana's Circle Society

The honor scholastic society of Louisiana State University School of Medicine, New Orleans, known as the Circle, was founded in the spring of 1940 to give recognition to students of unusual scholastic ability. The membership consists of 10 per cent of the senior class, three members of which are selected in their junior year. The senior members just recently elected are George A. Degenshein, Rudolph J. Marshall Jr., Charles D. Muller Jr., Morris Ruchelman and Malter A. Salatich. The new junior members of the Circle are Daniel W. Beacham, Norman Burnstein and Douglas Lindsey. The faculty advisers of the Circle this year are Drs. James D. Rives, professor of clinical medicine; Charles Midlo, assistant professor of anatomy, and Dr. Burns.

Annual Lectureship at Tennessee

The local chapter of Phi Beta Pi medical fraternity at the University of Tennessee College of Medicine, Memphis, has established an annual lectureship at the university. Each year some representative of a specialty will lecture to the student body and the Shelby County physicians. The initial speaker was Dr. Karl A. Menninger of Topeka, Kan., president of the American Psychiatric Association, who discussed "Personality Studies as a Function of the Private Physician."

Texas Fraternity Sponsors Lectures

The Alpha Nu chapter of Phi Rho Sigma medical fraternity at the University of Texas Faculty of Medicine, Galveston, has established the Phi Rho Sigma Lectureship in honor of deceased alumni of the chapter. The first lectures were delivered, December 1, by Dr. Rolla E. Dyer, chief, division of infectious diseases, U. S. Public Health Service, Washington, D. C., on typhus fever, and Dr. Russell L. Cecil, professor of clinical medicine, Cornell University Medical College, New York, on rheumatoid arthritis.

Sigma Xi Lecture

Under the auspices of the University of Cincinnati chapter of Sigma Xi, a lecture on bacterial nutrition as a tool in biologic chemistry was given at the college of medicine, January 29, by Milan A. Logan, Andrew Carnegie professor of biologic chemistry at the college of medicine. The lecture was open to the public.

Residents to Honor Dr. Barr

The resident physicians who had served under Dr. David P. Barr during the last seventeen years, at Washington University School of Medicine, St. Louis, at a recent dinner in Dr. Barr's honor, formed a committee to raise funds to have Dr. Barr's portrait painted. The chairman of the committee was Dr. Lee D. Cady and the treasurer, Dr. Leon Bromberg. The portrait has been finished and accepted by the committee which hopes to arrange a presentation ceremony soon for presentation of the protrait to the medical school. The artist was Mr. Charles F. Galt. The contributions to the fund have been to date exclusively from former house officers and interns who served with Dr. Barr. Dr. Barr recently became professor of internal medicine at Cornell University Medical College, New York. He is also a member of the Council on Pharmacy and Chemistry of the American Medical Association.

California Lectures to Students on War Medicine

The Committee on Medical School Curriculum of the University of California is sponsoring a series of lectures on war medicine to be given on Wednesdays from 3 to 4 p. m. at the University Hospital, San Francisco, constituting a voluntary course for third and fourth year medical students. Members of the faculty, the resident staff and the medical profession are cordially invited. The series will comprise the following lectures:

March 4, Burns; Replacement Therapy, Leon Goldman, assistant professor of surgery.
March 11, Wounds; First Aid to Injured; Orr or Trueta Treatment, H. Glenn Bell, associat professor of surgery.
March 18, Fractures as Related to the Army, LeRoy C. Abbott, professor of orthopedic surgery.
March 25, Fractures, Sprains, Care of Feet, LeRoy C. Abbott.
April 1, Head Injuries; Back Injuries; Peripheral Nerve Injuries, Howard C. Naffziger.
April 8, Infectious Diseases—Scarlet Fever, Diphtheria, Mumps, Measles—Under Wartime Conditions, Salvatore P. Lucas, associate professor of medicine.
April 15, Malaria, Syphilis, Plague, Cholera, Influenza, Dysentery, Typhus, Yellow Fever: Epidemiology and Prevention of These Diseases Under Wartime Conditions, Karl F. Meyer, Ph.D., professor of bacteriology.
April 22, Chemical Warfare; Gas Poisoning, Joel H. Hildebrand, Ph.D., professor of chemistry.
April 29, Vitamins and Nutrition, Gordon E. Hein, associate professor of medicine.
May 6, Aviation Medicine, Mayo H. Soley, assistant professor of medicine and pharmacology.

Hayden Scholars at Tufts

Dr. Cadis Phipps, professor of medicine and chairman of the scholarship committee at Tufts College Medical School, Boston, has announced the names of the first recipients of the recently established Charles Hayden Memorial Scholarships. These awards are made on the basis of individual need and promise to students who intend to enter general medical practice, and they average $250, which is applied to the first year tuition. The names of the first Hayden scholars at Tufts, all of whom had college degrees, follow:

Ward Allen Albro, Winchester
Frank Anthony Avola, Boston
George Raymond Bancroft Jr., Winchester
Louis Burke, Chelsea
Joseph Lewis Cafarella, Malden
Robert Cole Cornell, Mountain Lakes, N. J.
Brendan Forest Crotty, Jamaica Plain
Alfred Albert Delery, Somerville
Gordon Nichols French, Newton Centre
Leon Herman, Brighton
Francis Daniel McCarthy, Chelsea
David Edgar McGaw, Winthrop
George Benson McManama, Waltham
Stanley J. Mikalonis, South Boston
Edward Stephen Murphy Jr., Belmont
Morris Supowitz, Chelsea
John DeValera Sweeney, Waltham
George James Tsolas, Watertown
George Loughlin Tully Jr., West Newton
Lansing Pray Wagner, Wellesley
William John White, Jamaica Plain

Alpha Omega Alpha

A chapter of Alpha Omega Alpha, honorary medical society at Wayne University College of Medicine, Detroit, was installed, February 19, at a formal dinner. Dr. Walter L. Bierring, Des Moines, national president of Alpha Omega Alpha and Past President of the American Medical Association, and Dr. J. J. Moore of Chicago, the national secretary of the fraternity, were present. The criterion on which the granting of a charter is based at a medical school is the maintenance of the highest scholastic standards over a period of years. The nucleus of the new chapter was ten prominent members of the faculty of Wayne University. Future membership will come from the ranking 10 per cent of the senior class of medical students each June. Dr. Merritte W. Ireland, formerly surgeon general of the U. S. Army Medical Corps, presided at the dinner; the address was given by Dr. Louis B. Wilson of the Mayo Clinic, Rochester, Minn.

The following June graduates at the Western Reserve University School of Medicine, Cleveland, were elected to Alpha Omega Alpha:

Robert Reese Berneike
Paul Frederick Cooper
Walter Asahel Hoyt Jr.
Edward Joseph Humel Jr.
Harvey Krieger
Simour David Pomrinse
Salvatore Mario Sancetta
Edmund Frederick Schroeder
Austin Stanley Weisberger

The annual prize awards of this organization at Western Reserve have been made as follows:

Austin Stanley Weisberger, first prize, for his paper on "The Role of Specific and Nonspecific Serum Factors in Phagocytosis: A Study with Staphylococcus Aureus Hemolyticus."

Robert Edward Eckardt, second prize, for his paper on "Riboflavin, Its Assay, Distribution and Physiology."

The third prize was divided equally between Edward S. Rambousek, for his paper on "A Method for the Quantitative Analysis of Tin in Tissues," and Margaret Ruth Read for her paper on "Contribution to the Mechanism of Gastric Evacuation."

Harvard Renews National Scholarships

Harvard University, Cambridge, Mass., announced, October 19, the renewal of (THE JOURNAL, Sept. 27, 1941, p. 1134) national scholarships for the following medical students:

James S. Clarke '44, LaGrange, Ill.
Martin E. Flipse Jr., '44, Douglaston, L. I., N. Y.
Winsor C. Schmidt '44, Rye, N. Y.
Louis E. Ward '43, Mount Vernon, Ill.
Allan L. Friedlich Jr. '43, New York.
Glen R. Leymaster '42, Aurora, Neb.
Clarke T. Case '42, Pyinmana, Burma.
Laurence G. Wesson Jr. '42, Boston.

Society of Medical Sciences

At the annual banquet of the Louisiana State University Society of Medical Sciences, February 4, Mr. Louis Lazar was presented an award as the outstanding senior student of the year. Preceding the banquet Dan Beacham was elected president of the society for the coming year, Philip Cenac vice president and Richard Bates secretary-treasurer. The speakers at the meeting were Dr. E. L. Burns of the bacteriology and pathology department, Dr. Karl Dickens, the society's faculty adviser, and Dr. Connie Hood, a former president of the society.

Washington University Fraternity Sponsors Lecture

Dr. James Barrett Brown, associate professor of clinical surgery, Washington University School of Medicine, St. Louis, delivered the third annual Ephraim McDowell Lecture, March 3, at the Louisville City Hospital, Louisville, Ky., on "The Treatment and Skin Grafting of Burns." This lectureship is sponsored annually by the local chapter of the Phi Beta Pi medical fraternity of the University of Louisville School of Medicine.

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 1019:

1. Silas Weir Mitchell (1829-1914) of Philadelphia. Dr. Mitchell graduated from Jefferson Medical College in 1850 and spent the following year studying in Paris, where he came under the influence of Claude Bernard. His father was a physician, as were several other ancestors. With Surg. Gen. William A. Hammond in 1859 Mitchell investigated the arrow poisons corroval and vao and was the first, after Felice Fontana and Bonaparte, to investigate serpent venoms. In 1864 Mitchell, Morehouse and Keen published an important work on gunshot and other injuries of the nerves, which was translated into French and used in the French hospitals during the first world war. This work contains the earliest distinct accounts of ascending neuritis. Mitchell was the first to describe causalgia in 1864, erythromelalgia in 1872-1878 and postparalytic chorea in 1874. Mitchell introduced in 1875 a treatment of nervous disease by prolonged rest in bed, together with optimum feeding, massage and electricity, which came to be known as the Weir Mitchell treatment, or the "rest cure." His ideas were summarized in a classic monograph, "Fat and Blood," published in 1877 and translated into several foreign languages.

Mitchell was the author of one hundred and seventy-one medical papers on a variety of subjects, including neurology, toxicology, pharmacology and physiology. He was a commanding figure, a charming personality, and combined the high standards of the practitioner, investigator, clinician and research worker. In the world of letters Garrison places Mitchell near Goldsmith and Holmes and not far below Scott and Lamb. He was admired by all who knew him. Among his close friends were Holmes, Osler, Jacobi, Welch, DaCosta, Hammond and Billings.

Mitchell was awarded numerous national and international honors. He was a trustee of the University of Pennsylvania for thirty-five years. His patients came from many states to Philadelphia. He organized the library of the College of Physicians of Philadelphia, which through his efforts became one of the great medical libraries of the country. He contributed to the reform of methods of treating the insane. He, with DaCosta and Gross, founded the Philadelphia Pathological Society. His book "Hugh Wynne, Free Quaker," published in 1897, is one of the best historical novels in American literature.

2. Robert Watt (1774-1819). The Bibliotheca is a lasting monument to him, as it has been of great service to librarians and bibliographers. This stupendous task was practically complete when he died, but not entirely so until five years later. The idea seems to have originated in Watt's mind about the time he matriculated as a student in 1793. Watt studied medicine in Glasgow and was the first president of the Glasgow Medical Society. On his death the Faculty of Physicians and Surgeons gave his widow a pension of £45 a year, which she continued to draw until her death thirty-seven and a half years later. A daughter, the only surviving child, is said to have died in the poorhouse in 1864, and among her possessions were two sacks full of slips of paper, which turned out to be the manuscript of the Bibliotheca. The manuscript was purchased privately and presented to the Paisley Free Library, where the slips are now properly preserved and arranged in sixty-nine volumes—fifteen for authors and fifty-four for subjects. According to Monro's book "The Physician as Man of Science, Letters and Action," the Bibliotheca consists of four large quarto volumes, the first two containing the names of more than forty thousand authors with particulars of their work. The second part contains all the books mentioned in the first part arranged by subject.

Book Notices

Eye Hazards in Industry: Extent, Cause, and Means of Prevention. By Louis Resnick. Published for the National Society for the Prevention of Blindness. [New edition.] Cloth. Price, $3.50. Pp. 321, with 33 illustrations. New York: Columbia University Press, 1941.

The chances which American workmen take with such irreplaceable organs as eyes are a constant source of amazement to physicians and safety workers. Eye hazards in industry are in the majority of cases unnecessary. The author, Mr. Louis Resnick of the National Society for the Prevention of Blindness, who lived and died fighting this tragic waste, has assembled an overwhelming indictment against American industry and American workmen who persist in being careless about eye safety. According to his estimate, a painful eye injury occurs every thirty seconds, a total of more than three hundred thousand annually costing some $200,000,000 and more for all the attendant charges for treatment, compensation and rehabilitation which inevitably accompany these disabling accidents. Ninety-eight per cent of traumatic injuries to the eye are preventable, mainly through the simple device of protective goggles or eye shields. All the reliable methods of control are included in this book. Adaptation of personal and environmental protection to specific trades is amply illustrated in respect not only to solid foreign bodies but to exposure to radiant energy, chemicals and other toxic substances as well.

Trauma alone is not the only hazard to eyes in shops and mills. Almost as great a challenge is presented by the problem of detecting and correcting defective vision. It is clearly desirable to associate workmen with employment adapted to their physical abilities, and certainly eyesight must be given careful consideration. The question, then, of visual appraisal in industry is of great interest and importance. It seems sensible to recommend, and this book does, that the eyes of all applicants for work be examined, that placement in work occur according to the visual ability of the applicant with such correction as is necessary, and that consideration be given to the best ways by which employees can obtain glasses. Periodic eye examinations also should occur at varying intervals, depending on age and the severity of visual defects.

In addition, reliable information is given about standards for illumination in work places and for varying degrees of eye concentration. Certainly this aspect of better working conditions has been greatly neglected. Other sections of the book on education and supervisory methods of control, compensation data and the like give the same impression of careful and dependable preparation. Every page is an argument to shops and workmen everywhere who, in respect to eye injuries, say "It can't happen here!" It does happen and to the tune of one hundred totally blind and a thousand single eyes lost to workers, to industry and to society each year.

Soft Coal Miners' Health and Working Environment. By Robert H. Flinn, Passed Assistant Surgeon, United States Public Health Service, et al. From the Division of Industrial Hygiene, National Institute of Health. Prepared by direction of the Surgeon General. Federal Security Agency, U. S. Public Health Service. Public Health Bulletin No. 270. Paper. Price, 25 cents. Pp. 118, with 36 illustrations. Washington, D. C.: Supt. of Doc., Government Printing Office, 1941.

This bulletin is a report of a study of the physical condition of 545 soft coal miners and the health hazards of their working environment in three bituminous coal mines in Utah, conducted by the United States Public Health Service, Utah State Board of Health and other Utah state agencies. The physical evaluation of the miners included complete histories, examination and laboratory procedures indicated by type of exposure. The environmental studies were made in each mine to determine the health hazards of particular occupations. The results indicated that the dustiest occupations are associated with the underground operations. The dustiest occupations above ground were in the tipple, sand driers and dummy makers. The range was from 11,000,000 particles per cubic foot of air to 119,000,000. Petrographic studies showed 11 per cent free silica as the highest content, also that 83 per cent of the particles were less than 5 microns in diameter, the median being 1.94 microns. Exposure to gas, except to carbon monoxide immediately after blasting, did not occur.

Only data on miners with no other dust exposures were included in the results of the physical examination. Anthracosilicosis, a modified form of silicosis due to silica mixed with large amounts of carbon dust, was the principal occupational disease found. It may occur during the mining and processing of either anthracite or bituminous coal. Diagnosis was based on x-ray examination, symptoms and physical findings and the history of several years' exposure. Anthracosilicosis was found in 16 (3.2 per cent) of the 507 included. Fifteen of the 16 workers showed evidence of first stage involvement with but little disability; 1 worker showed evidence of second stage anthracosilicosis with moderate disability, and in no instance was third stage anthracosilicosis found. It was found only in workers whose principal occupation was underground. The incidence increased with increasing weighted average dust concentration and increasing duration of employment. The disease was not found among workers with less than ten years' employment in bituminous coal mines and was found in only 2 instances among workers with an average weighted dust exposure of less than 20,000,000 particles per cubic foot of air. As to dust concentrations above this level, duration of employment was important. The incidence of anthracosilicosis rose from 3.9 per cent in workers employed ten to nineteen years to 11.1 per cent in those employed twenty to twenty-nine years and to 50 per cent for the 12 workers employed thirty or more years.

The incidence of pulmonary tuberculosis was of minor importance, only 3 of the 507 workers showing minimal activity. Only one minimal healed lesion was found among workers with anthracosilicosis.

Other occupational hazards did not appear to be of significance. As a group, the health of these bituminous coal mine workers was found to compare favorably with that of workers in other dusty trades. There was improper sewage disposal in the mines and adjacent communities.

Directions for proper medical supervision and control of dust hazards are given.

Chemical Analysis: A Series of Monographs on Analytical Chemistry and Its Applications. Editorial Board: Beverly L. Clarke, I. M. Kolthoff, and Hobart H. Willard. Volume II: Chromatographic Adsorption Analysis. By Harold H. Strain, Ph.D. Cloth. Price, $3.75. Pp. 222, with 38 illustrations. New York: Interscience Publishers, Inc., 1942.

The technic of chromatographic adsorption analysis, a useful and relatively new tool of the modern investigator, was initiated in 1909 by the Russian botanist Tswett, who was interested in the nature of leaf pigments. Essentially, "chromatographic analysis" or "chromatography" involves a suitable adsorbent, such as talc, aluminum oxide or sugar, packed into an appropriate glass tube to form a column, through which may be aspirated a solution of the pigments under investigation. Owing to differences in the adsorptive properties of the pigments in the mixture, proper treatment with fresh solvent causes various colored bands to form in the column, each band denoting a particular pigment. Physical separation of the adsorbent column into its component colored zones, followed by elution of the adsorbed material, results in a separation of the pigments of the original mixture. The series of colored bands obtained during the process is called a "chromatogram." This name is somewhat poorly chosen, for in recent years the technic has been applied with success in the separation of many colorless substances.

In this book the author has collected for the first time the large amount of experimental data relative to chromatographic analysis which has accumulated since its inception. In a clear, concise style he discusses applications of the chromatographic method, the apparatus and technic involved, the selection, preparation and properties of the adsorbents employed and the selection and properties of solvents and eluants. Numerous diagrams of apparatus are provided. One chapter is devoted to the location of colorless adsorbed substances and another to the chromatography of inorganic compounds—relatively recent develments which are suggestive of future trends in this field. The chromatography of organic compounds is extensively discussed, with numerous references to original literature, in a chapter which illustrates the importance of this technic in the investigation of natural substances. A chapter on industrial applications is included. The book is an excellent summary of chromatographic adsorption analysis.

Operative Oral Surgery. By Leo Winter, D.D.S., M.D., F.A.C.D., Professor of Oral Surgery, New York University, New York. Cloth. Price, $10. Pp. 877, with 1,019 illustrations. St. Louis: C. V. Mosby Company, 1941.

As indicated in the foreword and elsewhere, this book is written primarily for the dental profession. Nevertheless, any one interested in oral surgery will find much information of value. The diagnosis and treatment of most of the common lesions about the mouth are well described, and many of the illustrations are excellent. There may be a superabundance in some instances, seventeen drawings being used to illustrate looping a circumferential wire around the lower jaw and twenty-three depicting the placing of a wire near the angle for external traction. Although two hundred and twenty pages are devoted to fractures of the jaws, less than two of these pages concern injuries of the upper jaw. The reader might gain the impression that maxillary fractures usually stop at the upper border of the alveolus, as no mention is made of their frequent extension through the antrum and the orbital floor. The treatment of condylar fractures also is omitted, though the author states that in his experience they have been the least frequent of mandibular breaks. The common minor operations about the mouth are well described and illustrated, but the possible hazards in some of the more formidable procedures are not discussed. For instance, in the description of open section of the ramus for ankylosis no mention is made of the considerable danger to the upper branches of the facial nerve. The treatment of carcinoma in and about the mouth is not included. The book should find wide use as a textbook for medical and dental students and for practitioners interested in the subject. The large number of instructive roentgenograms is one of its pleasing features.

Advances in Enzymology and Related Subjects. Edited by F. F. Nord and C. H. Werkman. Volume I. Cloth. Price, $5.50. Pp. 433, with 56 illustrations. New York: Interscience Publishers Inc., 1941.

This publication presents a collection of ten independent monographs devoted to special topics in enzymology: protein structure; Physikalisch-chemische Gesichtspunkte zum Problem der Virusaktivität; the specificity of proteinases; metabolic generation and utilization of phosphate bond energy; the chemical nature of catalase; enzymes and trace substances; photosynthesis, facts and interpretations; the bacterial photosyntheses and their importance for the general problem of photosynthesis; Untersuchung enzymatischer Prozesse in der lebenden Pflanze, and Die Verdauung bei den niederen Vertebraten. Each of these monographs is written by investigators who are recognized as authorities and have themselves contributed extensively to the original literature of the subject. No attempt is made to cover all the recent findings in the broad field of enzymology, but rather each of the selected topics is discussed from the point of view of its present day status. The scope of each subject covered is of a sufficiently limited character for it to be possible for each to be dealt with completely. The editorial policy closely resembles that of the German yearbook Ergebnisse der Enzymforschung. This is readily understood, since Dr. Nord was an editor of this publication. The text is free of both factual and mechanical errors. This volume is of primary interest to investigators in enzymology and the allied field of photosynthesis. However, the subject matter should attract the interest of many physicians, biologists and chemists.

Tratamiento moderno de las anemias. Por el Dr. A. H. Müller, médico director de la Sección de medicina interna del Hospital municipal de Glogau. Traducido del alemán por el Dr. J. Marín de Bernardo. Paper. Pp. 95. Madrid: Ediciones Morata, 1940.

This is a collection of twenty short essays intended principally for the general practitioner and dealing with the treatment of various types of anemia. The subject is exposed in the didactic lecture style, so that the reader is frequently confronted with categorical statements on controversial questions, inevitable in a work of this type. No formal classification of the anemias based on morphologic or pathophysiologic grounds is offered. The anemias are discussed principally from the standpoint of the disease with which they are associated, with the exception of addisonian pernicious anemia, which receives an adequate discussion from the pathophysiologic point of view. The principles of therapy advanced by the author are generally sound and in accordance with modern concepts, but many proprietary pharmaceutic preparations are recommended without any information being given concerning their composition. The literature cited is almost entirely German. The contributions of American authors on the subject of anemias of the addisonian and iron deficiency types are not given the proper prominence. Though nutritional factors are stressed when the author is dealing with anemias due to hemorrhage, no mention is made of the use of vitamin K. The book is useful for its quick, clear exposition of modern principles underlying the treatment of anemia, though its value is definitely impaired by the shortcomings mentioned.

Pathology of the Oral Cavity. By Lester Richard Cahn, D.D.S., Associate Professor of Dentistry (Oral Pathology), Columbia University, New York. Cloth. Price, $5.50. Pp. 240, with 166 illustrations. Baltimore: William Wood & Company, 1941.

This is a compact but inclusive treatment of the subject, with greatest emphasis on tumors and cysts, about one third of the book being devoted to them. About one fourth of the space is assigned to the discussion of the lesions of the mouth associated with systemic and general disturbances, such as avitaminoses, blood dyscrasias and endocrine disorders. Infections, dental caries, periodontal disease and pathologic changes of bone comprise the remainder. Nothing is included about actinomycosis and mercurial stomatitis; the treatment of the subject of hyperemia is not wholly satisfactory, chiefly because of failure to recognize the changes that are specifically associated with true hyperemia and congestion and the relationship of those conditions to clinical symptoms. Some minor slips occur, as on page 9, where it is stated that "viable polymorphonuclear leukocytes are resorbed back into the capillaries" instead of migrate back, and the use of the name Thomas instead of Thoma on page 127. The black and white illustrations are for the most part excellent and well chosen; there are selected references at the end of each chapter, and the index is satisfactory.

Index-Catalogue of the Library of the Surgeon General's Office, United States Army (Army Medical Library). Authors and Subjects. Fourth Series. Vol. VI.: G [Including] Third Supplement, Fourth Series: Bio-Bibliography of XVI. Century Medical Authors: Abarbanel-Alberti, Salomon. By Claudius F. Mayer, M.D. Cloth. Price, $2.75. Pp. 796; 52. Washington, D. C.: Supt. of Doc., Government Printing Office, 1941.

As a supplement to the Index Catalogue of the Army Medical Library, Dr. Claudius F. Mayer, editor of the Index Catalogue, has made available a "Bio-Bibliography of XVI. Century Medical Authors." The book appears with an extensive introduction. Here is an exceedingly important reference work for every person who is even slightly interested in medical history. In alphabetical order will become available the names of those who contributed to medical literature in the sixteenth century, with practically a complete list of books they have written and with a good deal of information as to the general character of these books and the various editions that have been published. The biobibliography will be condensed in subsequent volumes of the Index Catalogue. The present number covers only the material from Abarbanel to Alberti. For the more important authors there are reproductions of paintings, title pages of books and brief biographic notes.

Surgical Practice of the Lahey Clinic, Boston, Massachusetts. Cloth. Price, $10. Pp. 897, with 376 illustrations. Philadelphia & London: W. B. Saunders Company, 1941.

This book represents a cross section of Lahey Clinic surgical work as practiced today, its diagnostic measures, technics, methods and results. While the numerous papers published here have been recently published in various journals, this volume is not a mere compilation but is the product of the actual experience of Lahey Clinic members. The headings under which the surgical operations are discussed are the thyroid gland, esophagus and lungs, breast, stomach, duodenum and small intestine, biliary tract, colon, sigmoid and rectum, pelvis, kidney and prostate gland, bones and joints, brain, spinal cord and nerves, and anesthesia. The surgical methods followed, Dr. Lahey says, represent an attempt at such standardization as will permit each surgeon to perform each surgical procedure largely in the same way. The experience of the clinic has been that, as its staff has standardized operations, it has had improved end results and decreased mortality. Many of the surgical procedures and technics are well illustrated.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

SOLUBILITY OF SULFONAMIDE DERIVATIVES

To the Editor:—**Directions by the drug houses that make sodium sulfathiazole and sodium sulfapyridine are that the drug is to be dissolved only in distilled water. Dr. A. L. Hoyne, in a recent article on the treatment of meningitis (The Journal, Dec. 6, 1941, p. 1973), states that these drugs may be safely given in physiologic solution of sodium chloride but never in dextrose solution or blood transfusions. Can you tell me why it is dangerous to give these drugs in dextrose solution or in a blood transfusion?**

M.D., Louisiana.

ANSWER.—One of the big problems in sulfonamide therapy has been that of solubility of the compounds, and it is for this reason that the sodium salts have been prepared. Nevertheless there is always the fear that the drugs may not be completely dissolved, and the caution has been given that they should be dissolved in water. The statement that they should not be administered in dextrose solution or blood transfusion is probably based on the fact that the drugs might become less soluble in dextrose solution or blood than in water or saline solution alone. This opinion, however, is not shared by all observers, some of whom doubt that the danger is great when the sodium salts are used. Until the problem is completely solved, however, it is probably wise to use the drugs in aqueous solution rather than to run the risk of putting them in solutions in which there might be some loss of solubility.

CHRONIC CONSTIPATION AND ENTEROLITHIASIS

To the Editor:—**A woman aged 69 has been suffering from chronic constipation for decades. For the last six months or so she has been passing great amounts of intestinal gravel, consisting of magnesium and calcium phosphates and calcium carbonate. Is there any connection between chronic constipation and the formation of intestinal stones? Could you also kindly inform me as to the prevention and treatment of these calculi?**

Adolf Neustadt, M.D., Riverdale, N. Y.

ANSWER.—It is not known whether a relationship exists between chronic constipation and enterolithiasis. Blix (*Acta chir. Scandinav.* **76**:25, 1935) regarded intestinal stasis such as occurs proximal to a stricture or in a diverticulum to be the basic condition necessary for the formation of enteroliths in the small bowel. He further pointed out that the intestinal contents and their p_H influence the chemical composition of intestinal stones and, since these conditions are different at various levels of the bowel, different kinds of calculi may be formed. When an enterolith becomes dislodged and comes to rest in a lower segment of the bowel, the outer coating may then differ in chemical composition from that of the central portion. Blix's study was based chiefly on observations made on single large enteroliths recovered at operation and is not directly applicable to the case cited. Nevertheless it is of considerable interest in connection with the entire problem of enterolithiasis. It remains to be explained, however, why for each individual who has or passes intestinal stones there are many with apparently the same set of conditions in whom calculi are not found. Obviously the factors resulting in intestinal stone formation are not clearly understood at present. Consequently there is no satisfactory medical treatment.

The fact that in the case cited the stones consisted of magnesium and calcium phosphate and calcium carbonate suggests that they were formed in the colon or lower part of the ileum. It would be desirable, however, to know the quantitative as well as the qualitative analysis of the calculi, since these minerals have been detected in stones which consisted largely of some other constituent.

Although calculi formed within the lumen of the intestinal tract are usually considered to be uncommon, it has long been recognized that olive oil or similar substances taken by mouth may result in the appearance of concretions in the stool. Presumably these consist of insoluble soaps. They may bear some resemblance to gallstones, and this has led to the erroneous belief among some people that olive oil facilitates the passage of gallstones, an idea which has been exploited by some "patent medicine" manufacturers. Since olive oil is also taken at times to relieve constipation, it would be of interest to know whether the patient has taken it regularly during the past six months.

DEFICIENCIES IN PERNICIOUS ANEMIA

To the Editor:—**In an article entitled "Quantitative Treatment of Pernicious Anemia" in The Journal, Sept. 13, 1941 page 907, Askey states that liver is heat stable. Why was it recommended in the early days to be eaten raw or nearly so? Again he states: "It is probable that the liver is the only human organ in which it [the hemopoietic principle] is stored." I believe I am correct in stating that it is also found in the kidneys. Lilly's reticulogen has not been accepted for inclusion in N. N. R. The article states that those who received Lilly's liver extract were indicated with an asterisk. I failed to see any such mark. Again it is stated in a footnote that each cubic centimeter of reticulogen contained 100 international units of vitamin B_1; in another footnote the amount is boosted to 1,000 international units. Inclusion of this vitamin is responsible for the nonadmittance of this product. Most articles on pernicious anemia assume that if the reticulocyte count is satisfactory the patient needs no other treatment. I have not found this to be true. Patients suffer from diarrhea which has been attributed to the achylia, since it yields to the administration of dilute hydrochloric acid. I am of the opinion that crude liver extract—liver itself—is necessary in addition to the parenteral administration of liver extract, 15 U. S. P. units to the cubic centimeter. Patients complain of much flatus, tenesmus and a condition that corresponds to what the older clinicians termed enteralgia. The bouts come at intervals corresponding to relapse, but the blood picture is normal because of the parenteral injections. The patients improve on ingesting whole liver and dilute hydrochloric acid.**

Thomas I. O'Drain, M.D., Philadelphia.

ANSWER.—The main deficiency in pernicious anemia is a storage deficiency of a specific hepatic substance. This may be replenished either directly, by supplying material from other potent animal livers, or indirectly, by supplying other organs which, when given orally, act as building material for the eventual production of the specific substance. Thus bovine kidney and brain are effective when given orally but not when given parenterally. Desiccated hog's stomach is effective when given orally but not when given parenterally and is not heat stable.

The deficiencies in pernicious anemia are probably multiple. In addition to the shortage of the specific hepatic substance, there is undoubtedly vitamin B complex deficiency resulting from long-standing anacidity, deficiencies in diet and impaired absorption. A definite deficiency in thiamine is suggested by the therapeutic results of Zillhardt (Zillhardt, J. C.; Howard, Isabel, and Murphy, W. P.: *Ann. Int. Med.* **15**:33 [July] 1941). In cases of residual stationary neurologic findings, optimum liver therapy should be supplemented with adequate thiamine hydrochloride, given parenterally.

In treatment, many physicians prefer crude liver extract; others have found the concentrated extract quite satisfactory. Reticulogen was used in Askey's study because of its great concentration. Its vitamin B_1 content is 1,000 international units per cubic centimeter, not 100.

Two patients in the study who did not receive reticulogen were indicated by an asterisk (patients 16 and 18 in the table, after ages 84 and 66).

The added improvement resulting from the administration of whole liver and hydrochloric acid to a patient receiving adequate parenteral treatment is probably due not to a needed hemopoietic factor but probably to other vitamin factors in whole liver. Hydrochloric acid is of undoubted value in certain cases; in the majority it has proved unnecessary if optimum liver and vitamin therapy is given.

CEREBROSPINAL FLUID PROTEINS IN ACUTE POLIOMYELITIS

To the Editor:—**In acute anterior poliomyelitis it has been noted that during the period of recovery the total protein of the spinal fluid rises as the cell count falls. On the other hand, in the report of Viets and Warren (Acute Lymphocytic Meningitis, The Journal, Jan. 30, 1937, p. 357) it appears that in lymphocytic choriomeningitis the total protein of the spinal fluid rises and falls as the cell count rises and falls. Do these conditions occur regularly enough so that they can be used as a valid means of distinguishing the meningeal type of acute anterior poliomyelitis from lymphocytic choriomeningitis?**

Irving Kowaloff, M.D., Brooklyn.

ANSWER.—The reports are insufficient in number to justify the generalization that in acute anterior poliomyelitis during the period of recovery "the total protein of the spinal fluid rises as the cell count falls." The case reported by Ayer and Trevett (Acute Poliomyelitis with Choked Disks: Notes on Prolonged Observation of the Spinal Fluid and the Use of the Respirator, *Arch. Neurol. & Psychiat.* **31**:396 [Feb.] 1934), on which this statement is largely based, was observed for five months; both the pressure and the protein remained elevated. The patient was extensively paralyzed, including the muscles of respiration, but recovered in part, only to die within a year of pneumonia. This single case, complicated by a relapse and the presence of choked disks, cannot be considered as being typical of poliomyelitis.

No other patient has been observed with complete spinal fluid examinations as long as the one reported by Ayer and

Trevett. Most reports mention the condition of the spinal fluid at the end of three to six weeks after the onset of the disease. By that time the fluid is usually normal, but numerous instances have been reported in which the protein has remained elevated into the second and third months. One needs more reports of observations as long as the one of Ayer and Trevett; even examinations six to twelve months after infection would be justified to clear up the obscure point of how long the protein remains elevated in the average, not the exceptional, case.

Repeat examinations of the spinal fluid, even a year or more after the beginning of the disease, have been recorded in cases of acute lymphocytic choriomeningitis. Even in the acute stage, neither pressure nor protein is often much above normal; both fall rapidly to a normal level. If the data for poliomyelitis were as complete as those for lymphocytic choriomeningitis, some correlation between the two findings might be made. The two diseases, however, can usually be easily differentiated on other grounds; comparisons between the spinal fluids would hardly be a valid means of distinguishing one from the other in view of our present scant knowledge of the spinal fluid in poliomyelitis many months after the onset of the disease.

It should be pointed out, moreover, that in many instances specific antibodies may now be demonstrated in the blood in lymphocytic choriomeningitis and that virus identification by laboratory methods for both diseases is now available.

RADIOACTIVE PHOSPHORUS IN LEUKEMIA

***To the Editor:*—Is there available information on the new experimental treatment with energized phosphorus for lymphatic leukemia?**

John H. Henkin, M.D., Sioux City, Iowa.

ANSWER.—The question probably refers to the use of artificially induced radioactive phosphorus in the treatment of leukemia and in allied conditions such as lymphosarcoma and polycythemia. Radioactive phosphorus, which has an atomic weight of 32 instead of 31, the atomic weight of ordinary phosphorus, is produced by bombardment of ordinary red phosphorus in the cyclotron with the nuclei of heavy hydrogen, which are called deuterons. A neutron is captured by phosphorus 31, converting it into phosphorus 32, which is radioactive, emitting rather penetrating beta rays. In experiments on animals it was found that when phosphorus was first built into sodium phosphate and then injected into animals it concentrated in bone, leukemic and neoplastic tissues generally. It therefore seemed logical to use radioactive phosphorus as a form of selective radiation therapy in the treatment of leukemia, lymphosarcoma and allied diseases. The results obtained so far, extending over about four years, show that this method produces results which seem to be as good as those following roentgen or other treatment, but the work is still in the experimental stage. Present advantages seem to be the lack of any radiation reaction or sickness. Following are references describing some of the early investigations along this line:

Erf, L. A., and Lawrence, J. H.: Clinical Studies with the Aid of Radiophosphorus: III. The Absorption and Distribution of Radiophosphorus in the Blood of, Its Excretion by and Its Therapeutic Effect on Patients with Polycythemia, *Ann. Int. Med.* **15**: 277 (Aug.) 1941.

Lawrence, J. H.; Scott, K. G., and Tuttle, L. W.: Studies on Leukemia with the Aid of Radioactive Phosphorus, *Internat. Clin.* **3**: 33 (Sept.) 1939.

Erf, L. A.; Tuttle, L. W., and Lawrence, J. H.: Clinical Studies with the Aid of Radiophosphorus: IV. The Absorption of and Distribution of Radiophosphorus in the Blood of, Its Excretion by and Its Therapeutic Effect on Patients with Leukemia, *Ann. Int. Med.* **15**: 487 (Sept.) 1941.

LEG CRAMPS IN PREGNANCY

***To the Editor:*—I wish that you would discuss the cause and treatment of cramps of the leg during pregnancy. It is a minor symptom but sometimes causes the patient considerable discomfort.**

M.D., Michigan.

ANSWER.—Cramps or muscular contractions occur commonly in pregnant women. Cramps in the legs are especially frequent, often occurring during the night. They are more troublesome in the second half of pregnancy. There may be a connection between the cramps and lack of vitamin D and calcium. Hence increasing the vitamin D and calcium intake may decrease the incidence of cramps. During an attack massage helps; likewise, standing on a cold floor, such as the tile floor of a bathroom, usually relieves the muscular spasm. Frequent change of position in bed may help to prevent these cramps. Pains down the legs, shooting in character, often occur and are due to pressure of the baby's head on the nerves which go to the leg. These pains may be relieved by change of position, particularly a change to the knee-chest position.

THIAMINE HYDROCHLORIDE AND FURUNCULOSIS

***To the Editor:*—Please give an opinion as to the belief apparently held by some physicians that the use of thiamine hydrochloride predisposes to attacks of furunculosis. If there is any foundation for this belief, a brief discussion will be appreciated.**

E. S. Parker, M.D., Ida Grove, Iowa.

ANSWER.—There is no scientific foundation for the belief that the administration of thiamine hydrochloride under sterile precautions predisposes to attacks of furunculosis. Apparently the clinical incidence of thiamine and other vitamin B deficiencies is greater during the summer months than in any other period of the year. Likewise, the incidence of furunculosis and carbuncles is said to be higher during this period. The sole justifiable cause for the administration of thiamine hydrochloride is the evidence of a deficiency of this substance. It is usually recommended that the physician give the patient a well balanced diet irrespective of the administration of a specific vitamin preparation.

LYMPHATIC FLOW

***To the Editor:*—Kindly inform me if the lymphatic flow or current is always from the periphery to the center. Is it possible, in case of blocking a lymph tract, for the lymphatic flow then to establish a reversed flow?**

Marshall J. Payne, M.D., Staunton, Va.

ANSWER.—The last question is answered first: There can be no reversed flow without damage to the wall of the vessel. The question appears to be suggested by the occurrence of edema in an area where lymphatic drainage is blocked. This is due to accumulation of fluid and not to reversed flow.

It is not entirely clear what is meant by the phrase "periphery to center." In general, lymph channels tend to follow much the same course as veins, the entire flow finally entering the veins at the base of the neck. In limited areas there are often exceptions to the general direction of flow, but ultimately the rule holds.

CHANCES FOR PREGNANCY AFTER LONG PERIOD OF AMENORRHEA

***To the Editor:*—A woman aged 29 had two uneventful pregnancies, the last one being in 1934. She has not menstruated since 1938, apparently because of glandular disturbance. She is moderately obese but otherwise is in good health. Without treatment is there any further possibility of pregnancy? Is treatment indicated for any other reason?**

M.D., Iowa.

ANSWER.—The likelihood of a pregnancy during a long period of amenorrhea is rather remote. Usually ovulations do not occur. However, pregnancy is not impossible, for women can conceive during the amenorrhea of the postpartum period and during periods of secondary amenorrhea. Treatment is not indicated simply for the restoration of the menstrual function. Amenorrhea of this type may be the result of thyroid insufficiency, in which case there may be other signs of hypothyroidism which may call for treatment.

FUNGICIDES?

***To the Editor:*—Please advise me as to sodium orthobenzylphenol and sodium parabenzylphenol used as a preventive of ringworm. Also let me know as to any bad effects from the use of a combination of these solutions.**

Joseph A. Geis, M.D., Lake Placid, N. Y.

ANSWER.—A thorough search of the medical literature has revealed no reference to the fungicidal and fungicitic values of either sodium orthobenzylphenol or sodium parabenzylphenol. Without accurate mycologic studies it is impossible to give any opinion.

IS POLAR BEAR LIVER POISONOUS?

***To the Editor:*—With regard to the query in The Journal, January 24, R. L. Sutton Sr. and I spent several weeks of the summer of 1932 hunting bears and seals along the north coast of Spitsbergen. Our ship's crew of eighteen Norwegians were unanimously of the opinion that polar bear liver is poisonous both to man and to dogs. Ernst Sorensen of Tromso, our guide and interpreter, was a man of remarkable learning and accuracy of statement, intimately familiar with Spitsbergen history and polar exploration. From his personal knowledge he described to me instances of ill effects from ingestion of polar bear liver. Nausea, diarrhea and collapse were specified, along with emphasis on the appearance of erythema especially on parts exposed to sunshine. Judging from his words, I thought it likely that photosensitization might have been induced. I have seen no mention of this, however, in reading considerable literature dealing with photosensitization. I put several pounds of polar bear liver in mason jars, intending to investigate the matter, but during our travels before returning to the United States it seemed less and less desirable to carry the material in my suitcase, and I discarded it.**

Richard L. Sutton Jr., Kansas City, Mo.